

**LIGANDS FOR I7L AS MODULATORS OF ORTHOPOX VIRUSES AND
METHODS FOR DISCOVERY THEREOF
RELATED APPLICATIONS**

This patent application claims priority to provisional patent application Serial
5 No. 60/529,384, filed December 12, 2003. The disclosure of provisional patent
application Serial No. 60/529,384 is hereby incorporated by reference in its entirety.

FIELD OF INVENTION

The present invention relates to methods of discovery. The methods may be
advantageous for discovering compounds that alter a biological activity of a molecule
10 of interest. The present invention also provides anti-viral compounds that may be
identified using such methods.

BACKGROUND

Viruses are obligatory intracellular parasites that can take over host cell
transcription and translation to produce new viral particles. Interception of viral-
15 driven transcription or translation, including both pre- and post-translation events,
may result in crippling of the virus.

Smallpox, a member of the orthopox family of viruses, has recently
resurfaced as a public health concern. Until the last several years, the production of
vaccines and therapeutics to combat smallpox was not considered necessary, as the
20 last known case of smallpox was reported in 1977 in Somalia. In fact, universal
vaccination in the United States was discontinued in 1972, since the risk of
complications from the vaccine was actually greater than the risk of being infected
with the disease. As a result, a portion of the population has never been vaccinated
and thus, may be susceptible to infection by newly emerging strains of smallpox and
25 other orthopox viruses.

Small molecule chemotherapy may be an alternative to vaccination for the
prevention and/or treatment of orthopox viruses. For example, since the discovery of
non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors
(PIs), several classes of organic molecules have been designed to combat viral
30 infections by inhibiting targets responsible for viral replication and morphogenesis.
Due to the highly homologous nature of the orthopox family, therapeutics developed
against smallpox may also be potential candidate therapies for related viruses such as
monkeypox, a virus that recently reemerged in Africa and spread to the United States

by importation of exotic animals, and mulluscipox virus, a common cutaneous infection that may be problematic in immunocompromised individuals.

To date, no small molecule antiviral drug has proven to be effective in the treatment of smallpox. The only antiviral agent currently approved for use against
5 orthopoxviruses is cidofovir, a DNA polymerase inhibitor that may be used to treat cytomegalovirus and other herpes viruses. However, the usefulness of cidofovir may be limited in that the drug exhibits low bio-availability when administered orally, and thus, must be administered intravenously (Cundy, K.C., 1999, *Clin. Pharmacokinet.*, 36:127-143).

10 Because proteolysis catalyzed by viral-encoded proteases can be a necessary step in the development cycle of most viruses, protease inhibitors may provide another class of drugs that act as anti-viral agents. For example, protease inhibitors have proven to be effective against human immunodeficiency virus (HIV), influenza, hepatitis C, and rhinovirus enzymes.

15 During replication of vaccinia virus (VV), a prototypic member of the orthopox family, two types of proteolytic processing occur: formative and morphogenic. I7L is a protease involved in the maturation of the core protein of the orthopoxvirus virion. I7L appears to be involved in an obligatory morphogenic cleavage of three major structural proteins found in the mature VV virion: 4a, 4b, and
20 25K. I7L protease is a 47 kDa cysteine protease that contains putative catalytic histidine and cysteine residues embedded in a conserved region containing an aspartic acid residue. The gene for I7L appears to be highly conserved among poxviruses, as the identity among I7L genes between variola virus and vaccinia virus is 99%, and I7L genes from all orthopox viruses also appear to possess a large degree of
25 homology. The importance of I7L has been underscored in studies with temperature-sensitive (ts) viruses in which the I7L gene has been shown to be essential for viral replication using a conditional lethal mutant, *ts16*, that maps to this locus (Byrd, C.M., et al., *Virology*, 2003, 77:11279-11283; Byrd, C.M., et al., *Virology*, 2002, 76:8973-8976).

30 The resurgence of smallpox virus, and the threat of the use of smallpox virus as a weapon of biological warfare, has resulted in smallpox and other orthopox viruses reemerging as important public health concerns. The identification of agents that can either treat the symptoms caused by orthopoxviruses, or halt the spread of these viruses is of paramount importance. Thus, what is needed are methods for the

development of agents that may be used to target orthopoxviruses, such as smallpox. Such methods should allow for the rapid evaluation of large numbers of compounds such that the most effective compounds can be rapidly identified. In addition, such methods may provide a library of putative anti-viral agents. Such anti-viral agents
5 may reduce or remove the threat of the virus as a weapon, and may act as a strong deterrent to those attempting to develop pox viruses as biological weapons.

SUMMARY

The present invention relates to methods of discovery that may be embodied in a variety of ways. In an embodiment, the methods are useful for discovering
10 compounds that alter a biological activity of a compound of interest. The present also relates to these types of compound.

In one embodiment, the invention may comprise a method for identifying a compound having the ability to modulate virus propagation in a host cell. The virus may comprise an orthopox virus, such as smallpox virus, vaccinia virus, monkeypox
15 virus, mulluscipox virus, or cowpox virus. The method may comprise a first step of generating a three-dimensional model of a protein, or a portion thereof, required for orthopox viability. Next, a three-dimensional model of a potential modulator compound of interest may be generated. Finally, the method may comprise determining at least one atomic interaction between the potential modulator
20 compound and the protein, or a portion thereof, as defined by the three-dimensional models for each.

In one embodiment, the invention may comprise a method for identifying a compound that has the ability to modulate orthopox virus propagation in a host cell by inhibiting a viral I7L protease. The method may comprise the step generating a three-
25 dimensional model of I7L protein, or a portion thereof. The method may further comprise generating a three-dimensional model of a potential modulator compound of interest. Next, the method may comprise determining the nature of at least one of the atomic interactions between the potential modulator compound and the I7L protein, or a portion thereof, as defined by the three-dimensional models for the potential
30 modulator compound and I7L, protein or a portion thereof.

The present invention also provides a method of generating a three-dimensional model of a protein, or a portion thereof. The method may comprise the steps of providing an amino acid sequence of the protein of interest, and comparing the amino acid sequence of the protein of interest to the amino acid sequence of other

proteins for which a three-dimensional structure has been defined to identify a second protein having a predetermined level of sequence identity to the protein of interest.

Once a second protein having a known three-dimensional structure has been identified, the method may further include the step of aligning conserved residues
5 from the protein of interest with conserved residues from the second protein. Next, the sequence for the protein of interest may be threaded along the three-dimensional structure of the second protein, such that the position of at least two conserved residues from both proteins are aligned.

The present invention also comprises a computer model for I7L protein or a
10 portion thereof, comprising structural coordinates for a three-dimensional model for I7L protein, or a portion thereof, operable to be visualizable on a computer screen.

The present invention also provides anti-viral agents. In one embodiment, the anti-viral agents may inhibit poxvirus. The anti-viral agent may comprise a pharmacophore. For example, in one embodiment, the present invention may
15 comprise a pharmacophore comprising at least one atom or molecular group that interacts with at least one atom or molecular group of I7L protein, or a portion thereof. Or the anti-viral agent may comprise a compound. For example, in one embodiment, the present invention may comprise a compound comprising at least one atom or molecular group that interacts with at least one atom or molecular group of
20 I7L protein, or a portion thereof. In one embodiment, the compound interacts with I7L to modulate the activity of I7L. For example, the compound may be a compound identified by docking a computer representation of the compound, or a synthetic variant thereof, with a computer representation of a three-dimensional structure of I7L protein, or a portion thereof. In one embodiment, the three-dimensional structure of
25 I7L, or a portion thereof, is defined, at least in part, by Table 2. In yet another embodiment, the present invention may comprise a pharmaceutical composition. For example, the present invention may comprise a pharmaceutical composition comprising a compound identified by docking a computer representation of the compound with a computer representation of a structure of I7L protein, or a portion
30 thereof.

The present invention also comprises a method of conducting a drug-discovery business. The method may comprise the step of generating a three-dimensional structural model of a target molecule of interest on a computer. Also, the method may comprise generating a three-dimensional structural model of a potential modulator

compound of the target molecule on a computer, and docking the model for the potential modulator compound with the target molecule so as to minimize the free energy of the interaction between the target molecule and the potential modulator. In this way, a modulator compound that may interact with the target may be identified.

- 5 The method may also include the subsequent steps of providing a modified structure for the modulator compound of interest, and assessing whether the modified structure has a lower free energy of interaction with the target than the original modulator compound.

10 In another embodiment, the present invention comprises treatment of orthopox viral infections using compounds identified by the methods and systems of the present invention. The orthopox viruses may include smallpox virus or other orthopox viruses such as, but not limited to, vaccinia virus, monkeypox, or cowpox.

15 There may be advantages provided by certain embodiments of the present invention. For example, the methods of the present invention may provide a means to identify a plurality of putative pharmacological agents based upon the known three-dimensional structure of a target protein. Also, the present invention may provide a means to modify the structure of a putative pharmacological agent *in silico* to determine how such changes can effect the activity of the agent. Making such determinations *in silico* provides the ability to rapidly evaluate a large number of
20 compounds. Also, making such determinations *in silico* allows for a rational approach to drug development, such that compounds may be systematically developed and their activity evaluated.

The present invention may provide compounds that may be used as pharmaceuticals for treating humans and animals suffering from, or potentially
25 exposed to, infections caused by orthopox viruses, including smallpox, monkeypox and cowpox viruses. The compounds of the present invention may be used in combination therapy with other anti-viral agents. For example, anti-viral agents of the present invention that are protease inhibitors may be combined with other agents that act by other mechanisms. Also, the compounds of the invention may provide broad
30 spectrum antiviral agents with a low level of toxicity and a high therapeutic index. Such compounds may further provide an antiviral agent that may be used against viral strains that are resistant to other types of antiviral agents such as agents that inhibit DNA replication or immunomodulators.

There are, of course, additional features of the invention, which will be described in more detail hereinafter. It is to be understood that the invention is not limited in its application to the specific details as set forth in the following description and figures. The invention is capable of other embodiments and of being practiced or
5 carried out in various ways.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 shows a superposition of vaccinia virus (VV) I7L protease with the C-terminal domain of ULP1 protease in accordance with an embodiment of the present invention. I7L is shown as a solid ribbon and ULP1 is shown as a multi-lined ribbon.
10 Hang point residues of ULP1 (His514, Cys580, Trp448) and I7L (His241, Cys328, Trp168) are shown. Darker shading indicates regions of the polypeptide or individual residues that are closer to the viewer, whereas lighter shading indicates regions of the polypeptide or individual residues that are farther away.

FIG. 2 shows a three-dimensional homology threading model of vaccinia virus
15 (VV) I7L generated using the structure of the C-terminal portion of ULP1 protease in accordance with an example embodiment of the present invention. Darker shading indicates regions of the polypeptide or individual residues that are closer to the viewer, whereas lighter shading indicates regions of the polypeptide or individual residues that are farther away.

FIG. 3 shows a close-up view of the I7L ligand binding site in accordance
20 with an example embodiment of the present invention. Darker shading indicates regions of the polypeptide or individual residues that are closer to the viewer, whereas lighter shading indicates regions of the polypeptide or individual residues that are farther away.

FIG. 4 shows a computed docking mode of a small organic molecule, TTP-A,
25 on the surface of I7L protease in accordance with an embodiment of the present invention. TTP-A is shown in a meshed three-dimensional surface. Darker shading indicates regions of the polypeptide or individual residues that are closer to the viewer, whereas lighter shading indicates regions of the polypeptide or individual
30 residues that are farther away.

FIG. 5 shows a view of the I7L ligand binding domain in accordance with an example embodiment of the present invention wherein Leu324 is represented in a space-filling representation. Darker shading indicates regions of the polypeptide or

individual residues that are closer to the viewer, whereas lighter shading indicates regions of the polypeptide or individual residues that are farther away.

FIG. 6 shows the structure of two small molecule organic compounds, TTP-A and TTP-B, that bind to I7L protein, or a portion thereof *in silico* and that have an anti-viral effect in a cell culture assay in accordance with an example embodiment of the present invention.

FIG. 7 shows a method for identification of potential therapeutic compounds targeted to I7L using *in silico* screening and optionally, biological screening, in accordance with an embodiment of the present invention.

10 DETAILED DESCRIPTION

Definitions

The following definitions may be used to understand the description herein. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art. Practitioners are particularly directed to Current Protocols in Molecular Biology (Ansabel) for definitions and terms of the art. Abbreviations for amino acid residues are the standard 3-letter and/or 1-letter codes used in the art to refer to one of the 20 common L-amino acids.

I7L is a protease involved in the maturation of the orthopox virus virion and thus, is required for orthopox virus viability and/or replication. Vaccinia virus I7L is a 423 amino acid cysteine protease that catalyzes the cleavage of the 4a, 4b, and 25K structural proteins found in the mature vaccinia virus (VV) virion. The catalytic residues of wild-type I7L comprise a histidine and a cysteine embedded in a conserved region of the protein that contains an aspartic acid. I7L may be derived from a variety of sources, including orthopox viruses such as vaccinia virus, cowpox, camelpox, variola major, variola minor, monkeypox, ectromelia, sheeppox, lumpy skin, Yaba-like, swinepox, rabbit fibroma, myxoma, fowlpox, canarypox, armsacta moorei viruses. The enzyme may be from any source, whether natural, synthetic, semi-synthetic, or recombinant. A number of I7L proteins have been identified and cloned and these may be used in the methods of the invention. All of the I7L proteins characterized to date may be used in the methods of the present invention.

An I7L protein or part thereof in the present invention may be a wild type enzyme or part thereof, a mutant enzyme or part thereof, or variant or homologue of such an enzyme. As used herein, the term "wild type" refers to a polypeptide having

a primary amino acid sequence which is identical with the native enzyme. The term "mutant" refers to a polypeptide having a primary amino acid sequence which differs from the wild type sequence by one or more amino acid additions, substitutions or deletions. A mutant may or may not be functional. As used herein, the term "variant" refers to a naturally occurring polypeptide which differs from a wild-type sequence. As used herein, when referring to a protein, the terms "portion" or "part" indicate that the polypeptide comprises a fraction (or fractions) of the amino acid sequence referred to.

"Polypeptide" and "protein" are used interchangeably herein to describe protein molecules that may comprise either partial or full-length proteins.

As used herein, "small organic molecules" are molecules of molecular weight less than 2,000 Daltons that contain at least one carbon atom.

The term "vector" refers to a nucleic acid molecule that may be used to transport a second nucleic acid molecule into a cell. In one embodiment, the vector allows for replication of DNA sequences inserted into the vector. The vector may comprise a promoter to enhance expression of the nucleic acid molecule in at least some host cells. Vectors may replicate autonomously (extra chromosomal) or may be integrated into a host cell chromosome. In one embodiment, the vector may comprise an expression vector capable of producing a protein derived from at least part of a nucleic acid sequence inserted into the vector.

As used herein, the term "interact" refers to a condition of proximity between a ligand or compound, or portions or fragments thereof, and a portion of a second molecule of interest. The interaction may be non-covalent, for example, as a result of hydrogen-bonding, van der Waals interactions, or electrostatic or hydrophobic interactions, or it may be covalent.

As used herein, the term "atomic contacts" or "atomic interaction" refers to the inter-atomic contact between atoms in a test compound and atoms in a second molecule (e.g., the protein of interest) for which a three-dimensional model is made. The atomic interaction is governed by geometric and physiochemical complementarity as well as steric fit between the two molecules for which the atomic contacts/interaction is evaluated. Thus, an atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic. The atomic interaction may be covalent bond. For

example, atomic interactions between I7L ligand binding domain and small molecules TTP-A and TTP-B are described, at least in part, by Tables 5 and 6, respectively.

As used herein, the term "docking" refers to a process by which a test compound is placed in close proximity with a second molecule (e.g., the protein of interest). Docking is also used to describe the process of finding low energy conformations of a test compound and a second molecule (e.g., the protein or polypeptide of interest, or portion thereof). Docking studies include molecular modeling studies aimed at finding a proper fit between a ligand and its binding-site.

As used herein, the term "docking mode" refers to a favorable configuration of a test compound docked (e.g., positioned) within a given site on a molecule of interest.

As used herein, the term "hang point residues" refers to residues on a first molecule of known structure that are then used as anchors for the threading of a second molecule of unknown structure along the structure of the first molecule so as to determine a structure for the second molecule. For example, to determine a structure for I7L protein, or a portion thereof, residues Cys580, His514, and Trp448 of a ULP1 protein of known structure were the hang point residues that were aligned with Cys328, His241, and Trp168 of the I7L to determine the structure of I7L.

As used herein, the term "conserved residues" refers to amino acids that are the same among a plurality of proteins having the same structure and/or function. A region of conserved residues may be important for protein structure or function. Thus, contiguous conserved residues as identified in a three-dimensional protein may be important for protein structure or function. To find conserved residues, or conserved regions of 3-D structure, a comparison of sequences for the same or similar proteins from different species, or of individuals of the same species, may be made.

As used herein, the term "homologue" means a polypeptide having a degree of homology with the wild-type amino acid sequence. Homology comparisons can be conducted by eye, or more usually, with the aid of readily available sequence comparison programs. These commercially available computer programs can calculate percent homology between two or more sequences (e.g. Wilbur, W. J. and Lipman, D. J., 1983, *Proc. Natl. Acad. Sci. USA*, 80:726-730). For example, homologous sequences may be taken to include an amino acid sequences which in alternate embodiments are at least 75% identical, 85% identical, 90% identical, 95% identical, or 98% identical to each other.

The terms "identity" or "percent identical" refers to sequence identity between two amino acid sequences or between two nucleic acid sequences. Percent identity can be determined by aligning two sequences and refers to the number of identical residues (*i.e.*, amino acid or nucleotide) at positions shared by the compared sequences. Sequence alignment and comparison may be conducted using the algorithms standard in the art (*e.g.* Smith and Waterman, 1981, *Adv. Appl. Math.* 2:482; Needleman and Wunsch, 1970, *J. Mol. Biol.* 48:443; Pearson and Lipman, 1988, *Proc. Natl. Acad. Sci., USA*, 85:2444) or by computerized versions of these algorithms (Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive, Madison, WI) publicly available as BLAST and FASTA. Also, ENTREZ, available through the National Institutes of Health, Bethesda MD, may be used for sequence comparison. In one embodiment, the percent identity of two sequences may be determined using GCG with a gap weight of 1, such that each amino acid gap is weighted as if it were a single amino acid mismatch between the two sequences.

As used herein, a polypeptide or protein "domain" comprises a region along a polypeptide or protein that comprises an independent unit. Domains may be defined in terms of structure, sequence and/or biological activity. In one embodiment, a polypeptide domain may comprise a region of a protein that folds in a manner that is substantially independent from the rest of the protein. Domains may be identified using domain databases such as, but not limited to PFAM, PRODOM, PROSITE, BLOCKS, PRINTS, SBASE, ISREC PROFILES, SAMRT, and PROCLASS.

As used herein, "ligand binding domain" (LBD) refers to a domain of a protein responsible for binding a ligand. The term "ligand binding domain" includes homologues of a ligand binding domain or portions thereof. In this regard, deliberate amino acid substitutions may be made in the LBD on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the binding specificity of the ligand binding domain is retained. For example, for I7L protein, the ligand binding domain may comprise residues 110-423 of vaccinia virus I7L protein.

As used herein, the "ligand binding site" comprises residues in a protein that directly interact with a ligand, or residues involved in positioning the ligand in close proximity to those residues that directly interact with the ligand. The interaction of residues in the ligand binding site may be defined by the spatial proximity of the

residues to a ligand in the model or structure. The term "ligand binding site" includes homologues of a ligand binding site or portions thereof. In this regard, deliberate amino acid substitutions may be made in the ligand binding site on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the binding specificity of the ligand binding site is retained. For I7L, the ligand binding site may be defined as comprising those residues in Table 1. For example, the ligand binding site may be defined as comprising those residues in Table 1 and any other residues that are within a 3 angstrom radius of any one of the residues in Table 1.

As used herein, "catalytic domain" refers to a domain of a protein responsible for binding a substrate or that is involved in the catalytic mechanism. The term "catalytic domain" includes homologues of a catalytic binding domain or portions thereof. In this regard, deliberate amino acid substitutions may be made in the catalytic domain on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the binding specificity of the catalytic site within the catalytic domain.

As used herein, the "catalytic site" refers to a region of the catalytic domain that directly associates with a substrate or that is involved in the catalytic mechanism. For example, it may be a region of I7L that is responsible for binding a substrate.

With reference to the models and structures of the present invention, residues in a catalytic site may be defined by their spatial proximity to a substrate in the model or structure. The term "catalytic site" includes homologues of a catalytic site, or portions thereof. In this regard, deliberate amino acid substitutions may be made in the catalytic domain on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the substrate specificity of the catalytic site is retained. For example, for I7L, the catalytic site may be included as part of the ligand binding site to include at least some those residues listed in Table 1.

As used herein, a "ligand" refers to a molecule or compound or entity that associates with a ligand binding domain, including substrates or analogues or parts thereof. As described herein, the term "ligand" may refer to compounds that bind to the protein of interest. A ligand may be a modulator. Or, a ligand may not have a biological effect. Or, a ligand may block the binding of other ligands thereby inhibiting a biological effect. Ligands may include, but are not limited to, small

molecule inhibitors of the activity of protein. These small molecules may include peptides, peptidomimetics, organic compounds and the like. For proteases, ligands may also include polypeptide and protein substrates.

As used herein, a "modulator compound" refers to a molecule which changes
5 or alters the biological activity of a molecule of interest. A modulator compound may increase or decrease activity, or change the physical or chemical characteristics, or functional or immunological properties, of the molecule of interest. For I7L, a modulator compound may increase or decrease activity, or change the characteristics, or functional or immunological properties of the I7L, or a portion thereof. A
10 modulator compound may include natural and/or chemically synthesized or artificial peptides, modified peptides (e.g., phosphopeptides), antibodies, carbohydrates, monosaccharides, oligosaccharides, polysaccharides, glycolipids, heterocyclic compounds, nucleosides or nucleotides or parts thereof, and small organic or inorganic molecules. A modulator compound may be an endogenous physiological
15 compound or it may be a natural or synthetic compound. Or, the modulator compound may be a small organic molecule. The term "modulator compound" also includes a chemically modified ligand or compound, and includes isomers and racemic forms.

The terms "structural coordinates" or "atomic coordinates" as used herein
20 refers to a set of values that define the position of one or more amino acid residues or molecules with reference to a system of axes. A data set of structural coordinates defines the three dimensional structure of a molecule or molecules. Structural coordinates can be slightly modified and still render nearly identical three dimensional structures. A measure of a unique set of structural coordinates is the
25 root-mean-square deviation of the resulting structure. In alternate embodiments, structural coordinates that render three dimensional structures that deviate from one another by a root-mean-square deviation of less than 3 angstroms, or less than 2.0 angstroms, or less than 0.5 angstroms, or less than 0.3 angstroms, may be viewed by a person of ordinary skill in the art as identical. Variations in structural coordinates
30 may be generated because of mathematical manipulations of the structural coordinates of I7L as described herein. For example, the structural coordinates of Tables 2-4 may be manipulated by crystallographic permutations of the structural coordinates, fractionalization of the structural coordinates, integer additions or subtractions to sets of the structural coordinates, inversion of the structural coordinates or any

combination of the above. Variations in structure due to mutations, additions, substitutions, and/or deletions of the amino acids, or other changes in any of the components that make up a structure of the invention may also account for modifications in structural coordinates. If such modifications are within the standard error as compared to the original structural coordinates, the resulting structure may be considered to be the same or equivalent. Therefore, a ligand that bound to a ligand binding domain of an I7L would also be expected to bind to another ligand binding domain whose structural coordinates defined a shape that fell within the margin of error defined by the first structure. Such modified structures of a ligand binding domain are also within the scope of the invention. For example, using the surface topology of a group of ligands, such as low-energy binding modes of TTP-A and TTP-B, which exhibit effector quality (agonist or antagonist) can be overlapped and the contours of all TTP-A and TTP-B averaged into a union surface. This union surface of a ligand is expected to be complementary to the surface mold of the corresponding binding site of I7L enzyme.

As used herein, a structural "model" of a protein of interest, a polypeptide of interest, or any other compound of interest, may be in two or three dimensions. For example, a computer model may be in three dimensions despite the constraints imposed by a computer screen, if it is possible to scroll along at least a pair of axes, causing rotation of the image. Also, a model of a protein or chemical compound of interest may be defined by the structural coordinates for the protein or compound of interest.

As used herein, the terms "modeling" or "generating a model" includes the quantitative and qualitative analysis of molecular structure and/or function based on atomic structural information and interaction models. The term may include conventional numeric-based molecular dynamic and energy minimization models, interactive computer graphic models, modified molecular mechanics models, distance geometry, and other structure-based constraint models.

The term "substrate" refers to the molecule or compound that is the target of an enzyme. For I7L, a substrate may include proteins and polypeptides cleaved by the I7L protease and includes the 4a, 4b, and 25K structural proteins of vaccinia virus.

The term "peptide mimetics" are structures which serve as substitutes for peptides in interactions between molecules (Morgan et al., 1989, *Ann. Reports Med. Chem.*, 24:243-252). Peptide mimetics may include synthetic structures that may or

may not contain amino acids and/or peptide bonds but that retain the structural and functional features of a peptide, or agonist, or antagonist. Peptide mimetics also include peptoids, oligopeptoids (Simon et al., 1972, *Proc. Natl. Acad. Sci., USA*, 89:9367); and peptide libraries containing peptides of a designed length representing
5 all possible sequences of amino acids corresponding to a peptide, or agonist or antagonist of the invention.

The term "treating" refers to improving a symptom of a disease or disorder and may comprise curing the disorder, substantially preventing the onset of the disorder, or improving the subject's condition. The term "treatment" as used herein,
10 refers to the full spectrum of treatments for a given disorder from which the patient is suffering, including alleviation of one, most of all symptoms resulting from that disorder, to an outright cure for the particular disorder or prevention of the onset of the disorder.

As used herein, "TC50" is the concentration at which 50% of the cells display
15 signs of cytotoxicity. Also, "IC50" is the concentration at which there is 50% inhibition of the measured effect of interest. For I7L, "IC50" is the concentration at which there is 50% inhibition of viral cytopathic effect. The therapeutic index, "TI," is a ratio of the TC50 to the IC50. Thus, clinical beneficial drugs are generally those that have a high TI.

20 As used herein, "pharmacophore" is a collection of steric and electronic features that are necessary to ensure the optimal supramolecular interactions with a specific biological target structure. A pharmacophore may comprise a structural definition that comprises a set of active molecules. For example, using the surface topology of a group of ligands, such as low-energy binding modes of TTP-A and
25 TTP-B, which exhibit effector quality (agonist or antagonist) can be overlapped and the contours of all TTP-A and TTP-B averaged into a union surface that comprises a pharmacophore. This pharmacophore is expected to be complementary to the surface mold of the corresponding binding site of I7L enzyme.

As used herein, an "effective amount" as used herein means the amount of an
30 agent that is effective for producing a desired effect in a subject. The term "therapeutically effective amount" denotes that amount of a drug or pharmaceutical agent that will elicit the therapeutic response of an animal or human that is being sought. The actual dose which comprises the effective amount may depend upon the

route of administration, the size and health of the subject, the disorder being treated, and the like.

The term "pharmaceutical composition" is used herein to denote a composition that may be administered to a mammalian host, *e.g.*, orally, topically, parenterally, by inhalation spray, or rectally, in unit dosage formulations containing conventional non-toxic carriers, diluents, adjuvants, vehicles and the like. The term "parenteral" as used herein, includes subcutaneous injections, intravenous, intramuscular, intracisternal injection, or by infusion techniques.

The term "a" or "an" as used herein may refer to more than one object unless the context clearly indicates otherwise. The term "or" is used interchangeably with the term "and/or" unless the context clearly indicates otherwise.

Ligands for I7L as modulators of orthopox viruses

Embodiments of the present invention provide ligands for I7L as modulators of viruses and methods for discovery of such ligands. In one embodiment, the invention may comprise a method for identifying a compound having the ability to modulate orthopox virus propagation in a host cell. The method may comprise the steps of: (a) generating a three-dimensional model of a protein required for orthopox viability, or a portion thereof; (b) generating a three-dimensional model of a potential modulator compound of interest; and (c) determining at least one atomic interaction between the potential modulator compound and the protein, or a portion thereof, as defined by the three-dimensional models of each.

The virus may comprise an orthopox virus, such as smallpox virus, vaccinia virus, monkeypox virus, mullusciopox virus, cowpox virus, camelpox virus, variola major virus, variola minor virus, ectromelia virus, sheeppox virus, lumpy skin virus, Yaba-like virus, swinepox virus, rabbit fibroma virus, myxoma virus, fowlpox virus, canarypox virus, or amsacta moorei virus. In one example embodiment, the virus is smallpox virus. The protein may be any protein that is required for viability of the virus in a host cell. For example, the protein may be a protease that is required for formation or morphogenesis of the virus. Or, the protein may be required for DNA replication. The protein may be a cysteine protease. In one example embodiment, the protein is an I7L protease, such as vaccinia virus I7L protein.

The method may be performed using a computer. Thus, in one embodiment, the method comprises the steps of: (a) generating a three-dimensional computer model of the protein, or a portion thereof; (b) generating a three-dimensional

computer model of the potential modulator compound of interest; (c1) using a computer to dock the three-dimensional model of the potential modulator compound within the model of the protein or a portion thereof; and (c2) quantifying at least one atomic interaction between the potential modulator compound and the protein, or a portion thereof.

The method further allows for varying the structure of the potential modulator compound to determine how changes to the structure of the modulator may affect the fit of the compound with the protein of interest. Thus, the method may further comprise the steps of modifying the computer model of the potential modulator compound, and evaluating how modifying the computer model of the potential modulator compound changes at least one atomic interaction between of the model of the potential modulator compound and the model of the protein, or portion thereof. The potential modulator compound may be modified *in silico*. Thus, in one embodiment, the step of modifying the computer model of the potential modulator compound of interest comprises the step of searching a library of molecular structures for molecular fragments that can be linked to the potential modulator compound, wherein a molecular fragment comprises at least one atom. The method may further comprise linking a molecular fragment to the potential modulator compound to generate a modified compound. The modified compound may then be evaluated by docking the modified compound to the protein of interest and quantifying at least one atomic interaction between the modified compound and the protein of interest.

Also, the compound may be evaluated in a biological assay. Thus, the compound may be evaluated by its ability to inhibit virus growth or propagation. Also, the compound may be evaluated for cytotoxicity to uninfected cells. In one embodiment, the therapeutic index (TI), comprising the TC50 (concentration of the compound for which 50% of uninfected cells display signs of toxicity) divided by the IC50 (concentration at which the viral cytopathic effect is inhibited 50%) for the compound may be determined.

It may not be required to determine the entire structure of the protein of interest to identify compounds that may act as modulators of the protein. For example, the three-dimensional model of the protein of interest may comprise only a portion of the protein. Thus, the model may comprise the catalytic domain. Additionally or alternatively, the model may comprise a ligand binding domain. Additionally or alternatively, the model may comprise a ligand binding site.

Additionally or alternatively, the model may comprise the catalytic site. In some cases, the ligand binding site may also comprise the catalytic site.

It is also not necessarily required to determine how each amino acid of the entire structure of the protein of interest interacts with a potential modulator compound to identify compounds that may act as modulators of the protein. For example, the amino acid used to determine an atomic interaction between a potential modulator compound and the protein of interest may comprise a residue that is conserved in the protein of interest. Additionally, or alternatively, the amino acid used to determine an atomic interaction between a potential modulator compound and the protein of interest may comprise a residue that is present in, or affects the structure of, the catalytic domain and/or the catalytic site. Additionally, and/or alternatively, an amino acid used to determine an atomic interaction between a potential modulator compound and the protein of interest may comprise a residue that is present in, or affects the structure of, the ligand binding domain and/or the ligand binding site.

It has been shown that I7L protein (i.e., virion core protein proteinase) may be required for morphogenesis of orthopox viruses, and that without a functional I7L protein, propagation of the virus may be reduced. Thus, in one embodiment, the invention may comprise a method for identifying a compound having the ability to modulate orthopox virus propagation in a host cell, where the compound acts by inhibiting an I7L protease. The orthopox virus may comprise smallpox virus, vaccinia virus, monkeypox virus, mulluscipox virus, cowpox virus, camelpox virus, variola major virus, variola minor virus, ectromelia virus, sheeppox virus, lumpy skin virus, Yaba-like virus, swinepox virus, rabbit fibroma virus, myxoma virus, fowlpox virus, canarypox virus, or amsacta moorei virus. In one example embodiment, the virus is smallpox virus. The method may comprise the steps of: (a) generating a three-dimensional model of a I7L protein, or a portion thereof; (b) generating a three-dimensional model of a potential modulator compound of interest; and (c) determining at least one atomic interaction between the potential modulator compound and the I7L protein, or a portion thereof, as defined by the three-dimensional models of the I7L protein, or a portion thereof, and the potential modulator compound of interest.

The model of I7L may comprise a variety of formats. In one embodiment, the model may comprise a three-dimensional structural model. Or, the model of I7L may comprise structural coordinates presented as the position of individual atoms of the

I7L protein, or a portion thereof, in space. For example, the model of I7L, or a portion thereof, may comprise the x, y, and z atomic coordinates as defined in Table 2.

5 The model of I7L protein, or a portion thereof, may be derived at least in part from the structure of a protein that comprises a similar function to I7L. The method of generating the computer model may comprise aligning the structure of the I7L protein, or a portion thereof, with a second cysteine protease. In one example embodiment, the second cysteine protease is ubiquitin-like protein 1 (ULP1) protease.

10 The model of I7L may be derived at least in part by aligning conserved sequences from the I7L protein, or a portion thereof, and a second protein. In one embodiment, the amino acids used to align the structure of the VV I7L protein or a portion thereof with ULP1 comprise His241, Asp248, and Cys328 of the I7L protein and His 514, Cys 580 and Trp448 of ULP1.

15 The method may be performed using a computer. Thus, in one embodiment, the method comprises the steps of: (a) generating a three-dimensional computer model of the I7L protein, or a portion thereof; (b) generating a three-dimensional computer model of the potential modulator compound; (c1) using a computer to dock the three-dimensional model of the potential modulator compound with the model of the I7L protein, or a portion thereof; and (c2) quantifying at least one atomic
20 interaction between the potential modulator compound and the I7L as defined by the docking of the model of the potential modulator compound in the computer model of the I7L protein, or a portion thereof.

25 The method further allows for varying the structure of the potential modulator compound to determine how changes in the structure can affect the fit of the potential modulator compound with the protein of interest. Thus, the method may further comprise the steps of modifying the computer model of the potential modulator compound, and evaluating how modifying the computer model of the potential modulator compound affects the atomic interactions between of the model of the potential modulator compound and the model of the I7L protein, or portion thereof.
30 The potential modulator compound may be modified *in silico*. Thus, in one embodiment, the step of modifying the computer model of the potential modulator compound of interest comprises the step of searching a library of molecular structures for molecular fragments that can be linked to the potential modulator compound, wherein a molecular fragment comprises at least one atom. The method may further

comprise linking a molecular fragment to the potential modulator compound to generate a modified compound. The modified compound may then be evaluated by docking the modified compound to the I7L protein, or a portion thereof, and determining the atomic interactions between the modified compound and the I7L protein.

It is not necessarily required to determine the entire structure of the protein of interest to identify compounds that may act as modulators of the protein. For example, the three-dimensional model of the protein of interest may comprise only a portion of the protein. Thus, the model may comprise the catalytic domain, or a portion thereof. For example, the model may comprise the catalytic site. Additionally or alternatively, the model may comprise a ligand binding domain, or a portion thereof, such as the ligand binding site. For I7L, the ligand binding site may also comprise the catalytic site.

It may not be required to determine how each amino acid of the entire structure of the I7L protein interacts with a potential modulator compound to identify compounds that may act as modulators of the I7L protein. For example, an amino acid used to determine the atomic interactions between a potential modulator compound and the I7L protein may comprise a residue that is conserved in the I7L protein. Additionally or alternatively, the amino acid used to determine an atomic interaction between a potential modulator compound and the I7L protein may comprise a residue that is present in, or affects the structure of, the catalytic domain and/or catalytic site. Additionally, or alternatively, an amino acid used to determine an atomic interaction between a potential modulator compound and the I7L protein may comprise a residue that is present in, or affects the structure of, the ligand binding domain and/or ligand binding site.

The residues that are used to determine the atomic interactions between a potential modulator compound and the I7L protein may comprise an amino acid that is active in catalysis. In one example embodiment, the amino acids used to determine an atomic interaction between a potential modulator compound and the I7L protease, or a portion thereof, comprises the catalytic cysteine of the I7L protein. In one embodiment, the atomic interactions with the catalytic cysteine may comprise a charge or electrostatic interaction. Additionally, or alternatively, the amino acids used to determine an atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least one of Cys328, His241,

Asp248, or Asp258 of the I7L protein. Additionally, or alternatively, the amino acids used to determine an atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least one of Leu324, Trp242, or Gln322 of the I7L protein. Or, the amino acids used to determine an atomic
5 interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least one of Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln322, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203, or Met233 of the I7L protein. In one embodiment, the I7L protein, or portion thereof, is VV I7L.

10 Depending on the source of the protein used to generate a three-dimensional structure, there may be some variability in the absolute positioning of each amino acid. Still, it is to be expected that the relative positions of conserved amino acids may be maintained. For example, it has been found that there is a high degree in the catalytic triad sequence region (i.e., His241, Asp248, and Cys328 for VV I7L) of I7L
15 proteins isolated from various poxviruses (Byrd, C.M. et al., 2004, J. Virol., 78:12147-12156) Thus, alignment of sequences immediately surrounding amino acids in the catalytic triad may comprise 95-99 percent sequence identity and identical spacing between the residues. Thus, for I7L, the amino acids used to determine the atomic interactions between a potential modulator compound and the I7L protein may
20 comprise Cys(N), wherein position N corresponds to the catalytic cysteine. In one embodiment, the catalytic cyeteine corresponds to Cys328 of vaccinia virus I7L. Additionally, the amino acids used to determine the atomic interactions between a potential modulator compound and the I7L protein, or a portion thereof, may
25 comprise at least one of His(N-87), Asp(N-80), or Asp(N-70) of the I7L protein, wherein position N corresponds to the catalytic cysteine of the I7L. Additionally, the amino acids used to determine the atomic interactions between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least one of
30 Leu(N-4), Trp(N-86), or Gln(N-6) of the I7L protein, wherein position N corresponds to the catalytic cysteine of the I7L. Additionally, or alternatively, the amino acids used to determine the atomic interactions between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least one of Gly(N+1), Leu(N-5), Ser(N-88), Trp(N-160), Asp(N-134), Asn(N-157), Ser(N-155), Met(N-133), Ser(N-2), Glu(N-1), Leu(N-89), Leu(N-151), Asn(N-129), Met(N-159), Phe(N-

92), Ile(N-125) or Met(N-95), wherein position N corresponds to the catalytic cysteine of I7L.

The analysis may further employ a modified protein. Thus, the potential modulator compound may be evaluated for its interaction with a modified I7L protein, or portion thereof, wherein the I7L comprises at least one of an amino acid substitution, an amino acid deletion, or an amino acid insertion. In one embodiment, the amino acids used to determine the nature of the association between a test compound and the I7L protein, or a portion thereof, comprise at least one of wild-type or altered amino acid in the I7L protein corresponding to positions 168, 169, 171, 173, 177, 194, 195, 199, 203, 233, 236, 239, 240, 241, 242, 248, 258, 322, 323, 324, 326, 327, 328, or 329 of the wild-type VV I7L protein.

The nature of the interaction between the potential modulator compound and the protein of interest may be defined in terms of the atomic interaction between the compound and the protein of interest. In an embodiment, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic. Alternatively, the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, may comprise at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. Or, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. For example, for I7L, the atomic interactions between the modulator compound and I7L may comprise at least one of the atomic interactions described in Table 5. Or, the atomic interactions between the modulator compound and I7L may comprise at least one of the atomic interactions described in Table 6.

Also, the compound may be evaluated in a biological assay. Thus, the compound may be evaluated for inhibition of the virus. Also, the compound may be evaluated for cytotoxicity on uninfected cells. In one embodiment, the therapeutic index (TI), comprising the TC50 for the compound divided by the IC50 for the compound, may be determined.

The present invention also comprises a method of generating a three-dimensional model of a protein of interest, or a portion thereof. In one embodiment,

method may comprise the steps of: (a) providing an amino acid sequence of a protein of interest; (b) comparing the amino acid sequence of the protein of interest to the amino acid sequences of a plurality of other proteins; (c) identifying a second protein for which a three-dimensional structure has been defined, and that has a

5 predetermined level of sequence identity to the protein of interest; (d) aligning conserved residues from the protein of interest with conserved residues from the second protein; and (e) threading the protein of interest along the three-dimensional structure of the second protein such that the position of at least two conserved residues from both proteins are aligned.

10 The protein aligned with the protein of interest may also comprise a protein having a similar sequence to the protein of interest. The level of sequence identity may range from at least 5% sequence identity, to more than 10% sequence identity, to more than 20% sequence identity. Also, the protein aligned with the protein of interest may comprise a protein having a similar function as the protein of interest.

15 In one example embodiment, the protein of interest may comprise I7L and the second protein comprises ubiquitin-like protein 1 (ULP1). Where the protein of interest is I7L, and the second protein is ULP1, the amino acids used to align the structure of the I7L protein with ULP1 may comprise His241, Asp248, and Cys328 of the I7L protease, and His 514, Cys 580 and Trp448 of ULP1.

20 The present invention may also comprise a structural model for a protein, or a portion of a protein, that may be manipulated using a computer. In one example embodiment, the present invention may comprise a computer model for I7L protein, or a portion thereof. The model may comprise atomic coordinates for a three-dimensional model for I7L, or a portion thereof, operable to be visualizable on a
25 computer screen.

In one embodiment, the computer model of the protein of interest may comprise atomic coordinates presented as the position of individual atoms of the I7L protein, or a portion thereof, in space. For example, the model of I7L, or a portion thereof, may comprise at least some of the x, y, and z coordinates as defined in Table
30 2.

Also, the model may comprise a three-dimensional computer model of a potential modulator compound docked into the I7L structure such that the atomic interaction between the I7L and the potential modulator compound may be quantified. The atomic interactions between the I7L and the potential modulator compound may

be defined at least in part determining atomic coordinates for the potential modulator compound as it interacts with the I7L protein. In one embodiment, the three dimensional structure of a potential modulator compound may comprise at least some of the atomic coordinates as defined in Table 3 or Table 4.

5 The residues that are used to determine the atomic interactions between a potential modulator compound and the I7L protease may comprise an amino acid that is active in catalysis. In one example embodiment, the amino acid used to determine an atomic interaction between a potential modulator compound and the I7L protease, or a portion thereof, comprises the catalytic cysteine of the I7L protein. In one
10 embodiment, the atomic interactions with the catalytic cysteine may comprise a charge or electrostatic interaction. Or, an amino acid used to determine an atomic interaction between a potential modulator compound and the I7L protease, or a portion thereof, may comprise at least one of Cys328, His241, Asp248, Asp258 of the I7L protein. Or, an amino acid used to determine an atomic interaction between a
15 potential modulator compound and the I7L protease, or a portion thereof, may comprise at least one of Leu324, Trp242, or Gln322 of the I7L protein. Additionally, or alternatively, the amino acids used to determine an atomic interaction between a potential modulator compound and the I7L protease, or a portion thereof, may
20 comprise at least one of Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln 322, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203, or Met233 of the I7L protein. In one embodiment, the I7L protein, or portion thereof, is VV I7L.

 Depending on the source of the protein used to generate a three-dimensional structure, there may be some variability in the absolute positioning of each amino
25 acid. Still, it is to be expected that the relative positions of conserved amino acids may be maintained as there is a high degree in the catalytic triad sequence region (i.e., His241, Asp248, and Cys328 for VV I7L) of I7L proteins isolated from various poxviruses (Byrd, C.M. et al., 2004, J. Virol., 78:12147-12156) Thus, alignment of sequences immediately surrounding amino acids in the catalytic triad may comprise
30 95-99 percent sequence identity and identical spacing between the residues. Thus, for I7L, the amino acids used to determine the atomic interactions between a potential modulator compound and I7L protease may comprise Cys(N), wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the amino acids used to determine the atomic interactions between a potential modulator compound and the

I7L protein, or a portion thereof, may comprise at least one of His(N-87), Asp(N-80), Asp(N-70), of the I7L protein, wherein position N corresponds to the catalytic cysteine of I7L. Or, the amino acids used to determine the atomic interactions between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least one of Leu(N-4), Trp(N-86), or Gln(N-6) of the I7L protein, wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the amino acids used to determine the atomic interactions between a potential modulator compound and the I7L protease, or a portion thereof, may comprise at least one of Gly(N+1), Leu(N-5), Ser(N-88), Trp(N-160), Asp(N-134), Asn(N-157), Ser(N-155), Met(N-133), Ser(N-2), Glu(N-1), Leu(N-89), Leu(N-151), Asn(N-129), Met(N-159), Phe(N-92), Ile(N-125) or Met(N-95), wherein position N corresponds to the catalytic cysteine of I7L.

The computer model may further employ a modified protein. Thus, the potential modulator compound may be evaluated for its interaction with a modified I7L protein, or portion thereof, wherein the I7L comprises at least one of an amino acid substitution, an amino acid deletion, or an amino acid insertion. In one embodiment, the amino acids used to determine the nature of the association between a potential modulator compound and the I7L protein, or a portion thereof, comprise at least one of wild-type or altered amino acid in the I7L protein corresponding to positions 168, 169, 171, 173, 177, 194, 195, 199, 203, 233, 236, 239, 240, 241, 242, 248, 258, 322, 323, 324, 326, 327, 328, or 329 of the wild-type VV I7L protein.

The model may allow for the nature of the interaction between the potential modulator compound and the protein of interest to be defined in terms of the atomic interaction between the compound and the protein of interest. In an embodiment, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic. Alternatively, the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, may comprise at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. Or, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. For example, for I7L, the atomic interactions

between the modulator compound and I7L may comprise at least one of the atomic interactions described in Table 5. Or, the atomic interactions between the modulator compound and I7L may comprise at least one of the atomic interactions described in Table 6.

5 The model allows for varying the structure of the potential modulator compound to determine how changes in the structure of the modified compound can effect the fit of the compound with the protein of interest. Thus, the model may further comprise a three-dimensional model of a modified compound docked with the I7L structure. The potential modulator compound may be modified *in silico*. Thus, in
10 one embodiment, the step of modifying the computer model of the potential modulator compound of interest comprises the step of searching a library of molecular structures for molecular fragments that can be linked to the potential modulator compound, wherein a molecular fragment comprise at least one atom, and linking the fragments to the compound. The modified compound may then be evaluated by
15 docking the modified compound to the I7L protein, or a portion thereof, and determining the atomic interactions between the modified compound and the I7L protein.

 The present invention also comprises a pharmacophore having a structure required to modify the protein of interest. For example, the pharmacophore may
20 comprise at least one atom or molecular group that interacts with at least one atom or molecular group of I7L protein, or a portion thereof. Additionally, the three dimensional structure of the pharmacophore may comprise a plurality of atoms or molecular groups that interact with at least one atom or molecular group of a three-dimensional structure of I7L protein, or a portion thereof. To be active as a modulator
25 of I7L, the pharmacophore may interact with the ligand binding domain of I7L, or a portion thereof, such as the ligand binding site. Additionally or alternatively, the pharmacophore may interact with the catalytic domain, or a portion thereof such as the catalytic site of I7L.

 The structure of the pharmacophore may vary with changes in the structure of
30 the protein of interest. In one embodiment for I7L, the three-dimensional structure of I7L may be defined by at least some of the atomic coordinates as defined in Table 2. Where I7L is defined by the coordinates of Table 2, the spatial arrangement of atoms within the pharmacophore may comprise the atomic coordinates for at least one of the docking modes as defined in Table 3. In another example embodiment, the spatial

arrangement of atoms within the pharmacophore may comprise the atomic coordinates for at least one of the docking modes as defined in Table 4.

The nature of the interaction between the pharmacophore and the protein of interest may be defined in terms of the atomic interaction between the pharmacophore and the protein of interest. In an embodiment, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic. Alternatively, the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, may comprise at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. Or, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. For example, for I7L, the atomic interactions between the pharmacophore and I7L may comprise at least one of the atomic interactions described in Table 5. Or, the atomic interactions between the pharmacophore and I7L may comprise at least one of the atomic interactions described in Table 6.

The pharmacophore may be defined by its ability to interact with amino acids in the protein of interest that are important for catalytic activity and/or substrate binding. In one embodiment for an I7L pharmacophore, the interacting atom or molecular group for I7L may comprise the catalytic cysteine of I7L. In one embodiment, the atomic interactions with the catalytic cysteine may comprise a charge or electrostatic interaction. Or, the interacting atom or molecular group for I7L may comprise at least one of amino acids Cys328, His241, Asp248, Asp258, of I7L. Or, the interacting atom or molecular group for I7L may comprise at least one of amino acids Leu324, Trp242, and Gln322 of I7L. Additionally, or alternatively, the interacting atom or molecular group of I7L may comprise at least one of Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln 322, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203, or Met233 of the I7L protein. In an embodiment, the I7L, or a portion thereof, comprises VV I7L.

Depending on the source of the protein used to generate a three-dimensional structure, there may be some variability in the absolute positioning of each amino acid. Still, it is to be expected that the relative positions of conserved amino acids

may be maintained. As described above, there is a high degree in the catalytic triad sequence region (i.e., His241, Asp248, and Cys328 for VV I7L) of I7L proteins isolated from various poxviruses (Byrd, C.M. et al., 2004, J. Virol., 78:12147-12156). Thus, alignment of sequences immediately surrounding amino acids in the catalytic triad may comprise 95-99 percent sequence identity and identical spacing between the residues. For I7L, the interacting group(s) used to determine the atomic interactions between the pharmacophore and I7L protein may comprise Cys(N), wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the interacting group(s) may comprise at least one of His(N-87), Asp(N-80), Asp(N-70), of the I7L protein, wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the interacting group(s) may comprise at least one of Leu(N-4), Trp(N-86), or Gln(N-6) of the I7L protein, wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the interacting group of I7L may comprise at least one of Gly(N+1), Leu(N-5), Ser(N-88), Trp(N-160), Asp(N-134), Asn(N-157), Ser(N-155), Met(N-133), Ser(N-2), Glu(N-1), Leu(N-89), Leu(N-151), Asn(N-129), Met(N-159), Phe(N-92), Ile(N-125) or Met(N-95), wherein position N corresponds to the catalytic cysteine of I7L.

The computer model may further employ a modified protein. Thus, the pharmacophore may be evaluated for its interaction with a modified I7L protein, or portion thereof, wherein the I7L comprises at least one of an amino acid substitution, an amino acid deletion, or an amino acid insertion. In one embodiment, the I7L amino acids used to determine the nature of the association between the pharmacophore and the I7L protein, or a portion thereof, comprise at least one of wild-type or altered amino acid in the I7L protein corresponding to positions 168, 169, 171, 173, 177, 194, 195, 199, 203, 233, 236, 239, 240, 241, 242, 248, 258, 322, 323, 324, 326, 327, 328, or 329 of the wild-type VV I7L protein.

In yet another embodiment, the present invention comprises compounds that interact with at least one atom or molecular group of the I7L protein. In an embodiment, such compounds bind to the catalytic domain and/or catalytic site of I7L. In yet another embodiment, the compounds include molecules that interact with residues known to be in the ligand binding domain and/or ligand binding site. In yet a further embodiment, the compound comprises TTP-A or TTP-B.

The interaction between the compound and I7L may comprise an *in silico* interaction defined by a computer model of the structure of the compound and a computer model of the I7L protein, or a portion thereof. Thus, the present invention may also comprise a compound identified by docking a computer representation of the compound with a computer representation of a structure of I7L, or a portion thereof, as defined by Table 2. Where I7L is defined by the coordinates of Table 2, the spatial arrangement of atoms within the compound may comprise the atomic coordinates for at least one of the docking modes as defined in Table 3. In another example embodiment, the spatial arrangement of atoms within the compound comprises the atomic coordinates for at least one of the docking modes as defined in Table 4.

The nature of the interaction between the compound and the protein of interest may be defined in terms of the atomic interaction between the compound and the protein of interest. In an embodiment, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic. Alternatively, the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, may comprise at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. Or, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. For example, for I7L, the atomic interactions between the compound and I7L may comprise at least one of the atomic interactions described in Table 5. Or, the atomic interactions between the compound and I7L may comprise at least one of the atomic interactions described in Table 6.

The present invention also comprises pharmaceutical compositions comprising compounds able to modify the activity of a protein of interest. In one embodiment, the protein of interest may comprise I7L. Also, the pharmaceutical compositions may comprise anti-viral activity. In one embodiment, the present invention may comprise a pharmaceutical composition comprising a compound identified by docking a computer representation of the compound with a computer representation of a three-dimensional structure of I7L, or a portion thereof. The structure of I7L or a portion

thereof, may comprise at least some of the atomic coordinates as defined by Table 2. Also, the three dimensional structure of the compound used in the pharmaceutical composition may comprise at least some of the atomic coordinates of at least one of the docking modes as defined in Table 3. Or, the three dimensional structure of the compound used in the pharmaceutical composition may comprise at least some of the atomic coordinates of at least one of the docking modes as defined in Table 4.

The nature of the interaction between the compound of the pharmaceutical composition and the protein of interest may be defined in terms of the atomic interaction between the compound and the protein of interest. In an embodiment, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic. Alternatively, the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, may comprise at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. Or, the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, may comprise at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction. For example, for I7L, the atomic interactions between the compound able to modify I7L and the I7L protein may comprise at least one of the atomic interactions described in Table 5. Or, the atomic interactions between the compound able to modify I7L and the I7L protein may comprise at least one of the atomic interactions described in Table 6.

The compound may be defined by its ability to interact with amino acids in the protein of interest that are important for catalytic activity and/or substrate binding. In one embodiment for an I7L modulating compound, the interacting atom or molecular group for I7L may comprise the catalytic cysteine of I7L. In one embodiment, the atomic interactions with the catalytic cysteine may comprise a charge or electrostatic interaction. Or, the interacting atom or molecular group for I7L may comprise at least one of amino acids Cys328, His241, Asp248, Asp258, of I7L. Or, the interacting atom or molecular group for I7L may comprise at least one of amino acids Leu324, Trp242, and Gln322 of I7L. Additionally, or alternatively, the interacting atom or molecular group of I7L may comprise at least one of Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln 322, Met195, Ser326, Glu327, Leu239,

Leu177, Asn199, Met169, Phe236, Ile203, or Met233 of the I7L protein. In one embodiment, the I7L, or a portion thereof, is VV I7L.

Depending on the source of the protein used to generate a three-dimensional structure, there may be some variability in the absolute positioning of each amino acid. Still, due to the high homology maintained among I7L proteins from various sources at least in the catalytic triad region, it is to be expected that the relative positions of conserved amino acids may be maintained. For example, for I7L, the interacting group(s) used to determine the atomic interactions between the compound and I7L protein may comprise Cys(N), wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the interacting group(s) may comprise at least one of His(N-87), Asp(N-80), Asp(N-70), of the I7L protein, wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the interacting group(s) may comprise at least one of Leu(N-4), Trp(N-86), or Gln(N-6) of the I7L protein, wherein position N corresponds to the catalytic cysteine of I7L. Additionally, the interacting group of I7L may comprise at least one of Gly(N+1), Leu(N-5), Ser(N-88), Trp(N-160), Asp(N-134), Asn(N-157), Ser(N-155), Met(N-133), Ser(N-2), Glu(N-1), Leu(N-89), Leu(N-151), Asn(N-129), Met(N-159), Phe(N-92), Ile(N-125) or Met(N-95), wherein position N corresponds to the catalytic cysteine of I7L.

The compound may also be evaluated for its interaction with a modified I7L protein, or portion thereof, wherein the I7L comprises at least one of an amino acid substitution, an amino acid deletion, or an amino acid insertion. In one embodiment, the I7L amino acids used to determine the nature of the association between the compound and the I7L protein, or a portion thereof, comprise at least one of wild-type or altered amino acid in the I7L protein corresponding to positions 168, 169, 171, 173, 177, 194, 195, 199, 203, 233, 236, 239, 240, 241, 242, 248, 258, 322, 323, 324, 326, 327, 328, or 329 of the wild-type VV I7L protein.

The pharmaceutical composition may comprise the compound present in a therapeutically effective amount. In one embodiment, a therapeutically effective amount may comprise an amount sufficient to reduce a viral load in a subject. The dosage used for the pharmaceutical compositions of the present invention may vary depending on the specific compound being used, as well as the methods of administration. In one embodiment, a therapeutically effective amount may comprise a dose in a range from about 0.01 to 1,000 mg of active compound per kg body weight per day.

The pharmaceutical compositions and compounds of the present invention may be used to treat or prevent a variety of viral infections. The virus may comprise an orthopox virus, such as smallpox virus, vaccinia virus, monkeypox virus, mulluscipox virus, cowpox virus, camelpox virus, variola major virus, variola minor virus, ectromelia virus, sheeppox virus, lumpy skin virus, Yaba-like virus, swinepox virus, rabbit fibroma virus, myxoma virus, fowlpox virus, canarypox virus, or amsacta moorei virus. In one example embodiment, the virus is smallpox virus. Also, additional anti-viral agents may be employed.

The present invention also comprises a method of conducting a drug-discovery business. The method may comprise the step of generating a three-dimensional structural model of a target molecule of interest on a computer. Also, the method may comprise generating a three-dimensional structural model of a potential modulator compound of the target molecule on a computer, and docking the model for the potential modulator compound to with the target molecule so as to minimize the free energy of the interaction between the target molecule and the potential modulator. In this way, a modulator compound that may interact with the target may be identified. The method may also include the subsequent steps of providing a modified structure for the modulator compound of interest, and assessing whether the modified structure has a lower free energy of interaction with the target than the original structure for the modulator compound.

The method may further include evaluating at least some of the potential modulator compounds identified by *in silico* screening in a biological assay. Once compounds initially identified by the *in silico* assay are corroborated by a biological assay, animal studies may be used for detailed therapeutic profiling, and pharmaceutical compositions may then be developed. Or, additional *in silico* assays may be conducted on compounds that appear to be promising based on the biological data.

In another embodiment, the present invention comprises treatment of orthopox viral infections using compounds identified by the methods and systems of the present invention and pharmaceutical compositions comprising such compounds. The virus may comprise smallpox virus, vaccinia virus, monkeypox virus, mulluscipox virus, cowpox virus, camelpox virus, variola major virus, variola minor virus, ectromelia virus, sheeppox virus, lumpy skin virus, Yaba-like virus, swinepox virus, rabbit

fibroma virus, myxoma virus, fowlpox virus, canarypox virus, or amsacta moorei virus. In one example embodiment, the virus is smallpox virus.

The compound may comprise a small organic compound. In one example embodiment, the compound may comprise TTP-A, or a salt or prodrug thereof, as
5 defined herein. Or, the compound may comprise TTP-B, or a salt or prodrug thereof, as defined herein.

Structural Modeling of I7L

Embodiments of the present invention comprise computer modeling methods and systems to identify and optimize specific small molecules that bind to, and thus,
10 are able to modulate the activity of, a particular target protein. In one embodiment, the protein is I7L. Also provided by the present invention are compounds identified using the modeling methods described herein.

Thus, in one embodiment, the present invention provides a method of generating a three-dimensional model of a protein, or a portion thereof. The method
15 may comprise the steps of providing an amino acid sequence of the protein of interest and comparing the amino acid sequence of the protein of interest to the amino acid sequences of other proteins to identify a second protein for which a three-dimensional structure has been defined, and that has a predetermined level of sequence identity to the protein of interest. Once a second protein having a known structure has been
20 identified, the method may include the step of aligning conserved residues from the protein of interest with conserved residues from the second protein. Next, the sequence for the protein of interest may be threaded along the three-dimensional structure of the second protein such that the position of at least two conserved residues from both proteins are aligned. The conserved residues from the first protein
25 and the second protein may comprise residues that are essential for protein function.

Thus, as a first step, a three-dimensional model of the protein of interest may be generated. To generate a three dimensional model of a protein of interest, a sequence comparison to proteins with experimentally determined three-dimensional structures may be performed. The protein aligned with the protein of interest may
30 comprise a protein having a similar sequence to the protein of interest. The level of sequence identity may range from at least 5% sequence identity, to more than 10% sequence identity, to more than 20% sequence identity.

The protein aligned with the protein of interest may not necessarily be functionally related to the protein of interest. Or, the protein aligned with the protein

of interest may comprise a protein having a similar function to the protein of interest. In this way, conserved residues that have similar functions in the two proteins may be aligned.

5 In one embodiment, the protein of interest may comprise I7L. In performing structural modeling for I7L, a high sequence identity for vaccinia virus (VV) I7L is found with the C-terminal domain of another cysteine protease, Ubiquitin-like protease 1 (ULP1). ULP1 protease consists of 221 amino acids, and exhibits a 22% sequence identity with I7L. ULP1 may be used as a template for building the three dimensional model of I7L.

10 To develop a three dimensional structure for I7L, TTPredict™ site search algorithms may be used to identify the ligand binding site of I7L based on the location of active site residues His241, Asp248, and Cys328, that are known to be essential for I7L activity. Also, TTPredict™ algorithms may be used to identify known I7L-homologous sequences using BLAST searches on protein sequence databases.

15 TTPredict™ algorithms may also be used to access a number of publicly available and vendor supplied fold recognition programs to analyze I7L sequence folds (e.g., MSI suite of programs, TTPGene). Such sequence comparisons reveal that, as compared to other proteins with known 3D structures, the C-terminus domain of ULP1 (wwPDB Protein Data Bank Archive: PDB code:1EUV) has a high structural

20 homology to I7L sequence. The ligand binding domain of the I7L sequence (amino acids 110-423) may be mapped onto residues from the C-terminus of ULP1 protease domain using 3DPSM and the Homology modeling suites within the Accelrys suite of programs (San Diego, CA). Despite having only a 22% sequence identity with I7L, the 3D structure of ULP1 may be used as a threading template to generate a 3D model

25 for the I7L query sequence.

The threading approach may reveal distantly homologous proteins that share the same folding structure, but that do not comprise a high amount of sequence similarity. Rather than relying only on sequence alignment, the fold recognition method may blend the sequence-to-structure fitness with other structural

30 characteristics, such as sequence similarity and predicted secondary structures, to find conserved residues that appear in both the template protein of interest (e.g., I7L) as well as any query sequences, and overlay both sequences, maintaining alignment of the conserved residues. Next, the threading program may match the query sequence on the three-dimensional structure of the template using conserved residues of the

query protein as the hang points. The resulting model may then be cleaned-up using standard energy minimization and molecular dynamics techniques. In one embodiment, the conserved residues used as hang points may need to be determined *a priori*. FIG. 1 shows the results of the analysis for I7L and ULP1, wherein the hang point residues for ULP1 (His514, Cys580, and Trp448) are aligned with analogous and conserved I7L residues (His241, Cys328, Trp168) to generate a three-dimensional structure for I7L.

The present invention also comprises a computer-generated molecular model for I7L. For example, FIG. 2 shows a ribbon representation of I7L ligand binding domain based on alignment of the I7L protein sequence with ULP1 to generate a three-dimensional structure for the ligand binding domain of I7L. The model may comprise the catalytic site required for I7L-mediated cleavage of substrate proteins. The model may further include the ligand binding site for antiviral small molecule ligands. The predicted active site residues for I7L may include those residues that form the catalytic site, or residues that form the ligand binding site, or residues that participate in neighboring interactions required to maintain the structure of the ligand binding domain and/or the chemical functions required for the catalytic site. In FIG. 2, amino acid residues that comprise at least a part of the substrate binding pocket are labeled. Also, the predicted ligand binding site is shown within the oval shaped area.

The model may be further refined once the initial structural coordinates are defined. Thus, specific aspects of the model, such as the catalytic site and/or a ligand binding site, may be refined to incorporate the structures of substrates or ligands that may be bound at that site. I7L has two domains, a cysteine protease domain and a DNA regulatory domain. In the present invention, the cysteine protease domain was modeled, and is referred to as the ligand binding domain. The ligand binding domain thus includes the catalytic site, where substrate polypeptides are hydrolyzed, and a ligand binding site, where small molecule ligands bind. For example, FIG. 3 shows a detailed map of the I7L ligand binding site. It can be seen that Gln 322, Cys 328 (the catalytic cysteine), Trp168, Asn171, Asp194, Leu239, His241 and Asp258 line the ligand-binding site to some extent (FIG. 3). As shown in FIG. 3, the catalytic cysteine residue, Cys328, is located deep in the pocket. The Trp168 side chain protects the Cys328 residue from the solvent. Table 1 lists residues that may comprise the I7L ligand binding and catalytic site. In an embodiment, a more detailed

view, showing potential intramolecular interactions such as hydrophobic bonds, salt bridges and Van Der Waals interactions may be generated.

Table 1	
Predicted catalytic site residues of I7L	
Cys328, Leu 323, Leu324 , His241 , Ser240, Trp168, Asp194, Asp258, Trp242 , Asp248, Asn171, Ser173, Gln 322 , Met195, Cys237, Leu239, Leu177, Met233, Ile332, Ile174, Lys175, Leu198, Phe234, Gln192, Ile161	

5 The structure of I7L may be defined by a graphic two-dimensional figure of a three-dimensional model as shown in FIGS. 1-3. The representations shown in FIG. 1-3 may also be viewed on a computer screen. When visualized on the computer, the models may be rotated to provide multiple views. For example, the viewer may rotate the model so as to provide a view that is rotated to the right or the left of the views shown in FIGS. 1-3. Or, the models depicted as FIG. 1-3 may be used to form a physical model.

10 Additionally, the structure of the I7L protein, or a portion thereof, may be defined by the atomic coordinates in three dimensional space. Table 2 provides the three-dimensional atomic coordinates for the I7L ligand binding domain, wherein the position of each atom is defined by a unique x, y, and z coordinate in three dimensional space. Shown in Table 2, is the identity of the atom (column 3), the amino acid and residue number (cols. 4 and 5), and the actual coordinates for each atom in x, y, and z dimensions (cols. 6, 7, and 8, respectively. As described herein, a data set of structural coordinates defines the three dimensional structure of a molecule or molecules. Structural coordinates can be slightly modified and still render nearly identical three dimensional structures. A measure of a unique set of structural coordinates is the root-mean-square deviation of the resulting structure. In alternate embodiments, structural coordinates that render three dimensional structures that deviate from one another by a root-mean-square deviation of less than 3.0 angstroms, or less than 2.0 angstroms, or less than 0.5 angstroms, or less than 0.3 angstroms, may be viewed by a person of ordinary skill in the art as identical or equivalent.

In Silico Screening Of Putative I7L Modulators

The present invention further provides methods to dock compounds of interest, such as putative therapeutic agents, into the structure of the modeled protein to determine whether such putative therapeutic agents may interact with the protein. In one embodiment, the protein of interest is I7L protein, and the putative therapeutic agents are putative modulator compounds. For example, the modulator compounds may act as anti-viral agents. Thus, the putative therapeutic agents may bind to the ligand binding site and/or catalytic site to modify I7L activity.

To generate a three dimensional model of a potential modulator compound of interest, or a plurality of potential modulator compounds, a database of *in silico* structures for potential modulator compounds of interest, such as provided by TTProbes™, may be used. Once the three-dimensional structures of the modulator compounds of interest have been generated, the compounds may be docked into the ligand binding site of the protein of interest.

For example, in one embodiment, the site tested for interaction with potential modulator compounds being tested for anti-viral activity may comprise the ligand binding domain of I7L as described by the three-dimensional model. The amino acids which are assessed for interaction with the test compounds may comprise amino acids involved in catalysis, such as Cys328 of the VV I7L protein. Many of the residues relevant for I7L catalytic activity appear to be located in the immediate vicinity of the ligand binding site as defined by the three-dimensional model of the present invention. For example, in one embodiment, amino acids important for catalytic activity are included within a 3 angstrom radius of the residues in Table 1.

Additionally or alternatively, the amino acids important for catalytic activity are included within a 3 angstrom radius of the catalytic cysteine, histidine, and/or aspartate in the catalytic triad. For example, there are several conserved amino acids, including Ser240, His 241, Trp168, Trp 242, Asp 248, Asp 258, Gln 322, Cys 328, and Gly 329, that may be relevant for I7L catalytic activity. Also, compounds may be specifically tested for their ability to interact *in silico* with Cys328 as the catalytic cysteine. For I7L, the amino acids assessed for putative interactions with test compounds may include at least some of the amino acids listed in Table 1. In one example embodiment, the amino acids tested for interaction with the test compound may comprise His 241, Trp 242, Asp 248, Asp 258, Gln 322, Cys 328, Gly 329,

Leu324, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203, and/or Met233 of the vaccinia virus I7L.

The putative therapeutic agents may comprise a variety of compounds. In one embodiment, the putative therapeutic agent may comprise a peptide or a peptidomimetic. Or, the putative therapeutic agent may comprise an antibody. Alternatively, the putative therapeutic agent may comprise a small organic compound.

FIG. 4 shows a docking mode of a small organic compound with the I7L ligand binding domain. The compound shown docked in the ligand binding domain of I7L is 3-hydroxy-naphthalene-2-carboxylic acid [2-(2-methoxy-4'-nitro-biphenyl-3-yl)-ethyl]-amide (TTP-A). TTP-A is shown as a meshed surface. It can be seen that one end of TTP-A makes contact with the catalytic cysteine (Cys328) and histidine (His241) residues and at least some of the other catalytic residues listed in Table 1. A similar compound, 3-(3'-chloro-4'-fluoro-biphenyl-4-yl)-2-[(4-hydroxy-4'-trifluoromethyl-biphenyl-3-carbonyl)-amino]-propionic acid methyl ester, (TTP-B), and other similar active analogs, make canonical contacts with active site residues of I7L protease.

The structure of a putative ligand may be provided as a three-dimensional space-filling model, as a rotatable model on a computer screen, or as atomic coordinates in three-dimensional space. In one embodiment, the compounds that dock into the ligand binding site with a negative free energy are considered to be favorable. In alternative embodiments, a compound having an free energy of interaction with I7L (or another molecule of interest) of less than -2 kcal/mol, or less than -5 kcal/mol, or less than -10 kcal/mole, are considered to provide favorable binding to the protein of interest. For example, Tables 3 and 4 provides the coordinates for several computed low-energy docking modes for TTP-A and TTP-B, respectively. For TTP-A, the energy of interaction is about -11.24 kcal for all five docking modes. For TTP-B, the energy of interaction ranges between -8.81 kcal/mol to about -10.68 kcal/mol for the five low-energy docking modes.

Thus, the three-dimensional coordinates as listed in Tables 3 and 4 provide the low energy structures of TTP-A and TTP-B, respectively, as each compound interacts with I7L. The low-energy docking modes for TTP-A as provided in Table 3, and for TTP-B as provided in Table 4, may favor interactions with at least some of the I7L residues listed in Table 1. In Tables 3 and 4, from the left, the second column

identifies atom number, the third column identifies atom type, the fifth column identifies the docking mode (i.e., 1-5) the sixth column identifies the x coordinates, the seventh column identifies y coordinates, and the eighth column identifies the z coordinates.

5 In one example embodiment, TTP-A, TTP-B, and their derivatives, bind to the same binding surface of the I7L model. For example, in the predicted docking with I7L, active therapeutic compounds will make favorable contacts with at least some of the residues shown in Table 1. As the residues identified in Table 1 appear to be required for catalytic activity, it may be of importance that the putative therapeutic
10 agent recognizes the binding surface that is described in Table 2 and at least some of the residues as described in Table 1 to provide the potential inhibit the cysteine protease activity of I7L.

 The molecular model may be further corroborated by studies of drug-resistant mutants. For example, in one embodiment, a drug-resistant virus may be isolated by
15 passaging of the virus in the presence of the drug of interest. For example, a vaccinia virus passaged in the presence of TTP-A may, after several passages, result in the emergence of a viral strain that exhibits resistance to the inhibitory effects of TTP-A. The resistant virus may be isolated, and the I7L gene sequenced to determine whether resistance is due to a change of the I7L protein, such that the TTP-A is no longer as
20 effective therapeutically. In one embodiment, passaging of the virus in the presence of TTP-A may result in a mutation of the I7L protein. For example, passage of vaccinia virus in the presence of TTP-A may result in mutations in certain positions of the protein. In alternate embodiments, there may be a Y to C mutation at position 104 of the I7L protein, and an L to M mutation at 324 of the I7L protein. FIG. 5 shows a
25 model of the I7L active site showing that the position of Leu324 is in close proximity to the catalytic cysteine, Cys328.

 Tables 5 and 6, list the nature of several atomic interactions for TTP-A and TTP-B, respectively, with atoms in the I7L protein. Thus, Tables 5 and 6, identify groups on I7L, as defined by Table 2, that interact with the designated atom on TTP-
30 A or TTP-B, as defined by the first docking mode of either Table 3 or Table 4, respectively. By comparing the relative coordinates of the I7L residues to the coordinates of the atoms in the first docking modes for TTP-A and TTP-B, the distance between the atoms and the type of interaction may be determined. The

structures of TTP-A and TTP-B, with the numbering of atoms for each molecule as used in Tables 5 and 6, are shown in FIG. 6.

The molecular model may be used in a computational assay by which virtual ligands are inserted into the active site to identify those agents having the highest potential to bind to, and/or modify, the I7L activity. In a further embodiment, the compounds identified by molecular modeling are tested in a biological assay. For example, compounds may be evaluated to determine whether the compound displays cytotoxic effects on uninfected cells. Additionally, the compound may be evaluated to determine the amount of compound that exhibits an inhibition of cytopathic effect (CPE) of the virus.

The results of the determination of cytotoxicity may be compared to the effectiveness of the compound as an anti-viral agent, to determine the therapeutic index (TI) of the compound. The 50% inhibitory concentrations (IC₅₀), measured as the concentration of the compound that results in inhibition of the viral cytopathic effect (CPE) for 50% of treated cells, and the 50% toxicity concentration, measured as the concentration of the compound at which 50% of uninfected cells display signs of cytotoxicity (TC₅₀), may be compared, and the therapeutic index calculated as the value of TC₅₀ divided by IC₅₀.

The results of the biological assay may provide further data which can be used in the next round of molecular modeling. For example, compounds that display a large therapeutic index may be further modified *in silico* to attempt to improve the effectiveness of the compound and then reevaluated by a biological assay. The process may be repeated until a compound maximal TI is identified. In addition, the compound may be further developed by animal testing and formulation of an appropriate pharmaceutical composition.

In addition to a cell culture assay, a molecular assay of the effectiveness of the compounds identified by *in silico* screening may be performed. For example, the ability of a candidate compound such as TTP-A may be evaluated by determining whether the compound inhibits proteolysis of a I7L substrate, such as the P4b precursor protein, by I7L. Such molecular assays may provide evidence that the compound of interest is targeting the protein of interest to inhibit catalysis. If inhibition of cleavage of the substrate is not observed, it may indicate that the compound identified by *in silico* screening is acting at a different point of the viral formative and/or morphogenic cycle.

A schematic of a method used to develop anti-viral agents is shown in FIG. 7. Thus, the method may include a first stage 100 of developing a three-dimensional model of a protein or polypeptide of interest (e.g., viral I7L). As described herein, the method may comprise providing the amino acid sequence for the protein or polypeptide of interest 110. The sequence of the protein or polypeptide of interest may then be compared to amino acid sequences available in protein sequence databases 120 to identify proteins or polypeptides that have a known structure, and that may be homologous in structure to the protein or polypeptide of interest 130. If a second polypeptide or protein of known structure that has a sequence that includes regions of identity to the protein or polypeptide of interest is identified, the second protein may be used to align conserved residues from the second protein or polypeptide with the first protein or polypeptide of interest 140. The aligned residues (hang-points) may then be used as anchors as the first polypeptide or protein of interest is threaded along the structure of the second protein or polypeptide of interest to construct a three-dimensional model of the first polypeptide or protein of interest 150.

Once a three-dimensional model of the protein or polypeptide of interest has been constructed, it may be used in an *in silico* assay for screening a plurality of compounds 200. The *in silico* assay may comprise generating a library of three-dimensional structures for potential therapeutic agents 210. For example, in one embodiment a library of small high information density organic molecules (i.e., a library, wherein each small molecule within the library contains at least one functional group of interest) may be prepared. Such a library is provided by TTProbes™ (TransTech Pharma., Inc., High Point, NC) which is a set of more than 51,000 pharmacophorically diverse molecules of high information density. The *in silico* probes may then be docked into the three-dimensional structure of the protein or polypeptide of interest as described herein to determine the atomic interactions between the protein/polypeptide and the compound 220. Optionally, the compound may also be modified by adding or removing molecular fragments from the compound 230, and then the modified compounds docked into the three-dimensional structure of the protein or polypeptide of interest 240 to determine how the changes to the structure of the compound may affect the interaction of the compound with the protein/polypeptide. Such molecular alterations may be made until there is no longer

an apparent improvement in the ability of the compound to interact with the polypeptide/protein of interest. For example, for I7L, and using the TTProbes™ *in silico* library, over 3,000 candidate potential I7L modulators were identified. The method may include the option 299 of developing the compounds identified by *in silico* screening, or, performing further testing of the compounds by a biological assay.

Thus, still referring to FIG. 7, the putative therapeutic agents (i.e., potential modulator compounds) identified by *in silico* screening may then be evaluated by other types of assays for biological activity 300. For example, a putative receptor ligand may be evaluated using a binding assay. For putative anti-viral agents, the compounds may be evaluated to determine whether they inhibit viral growth and propagation 310. Also, the compounds may be evaluated to determine whether they are toxic to uninfected cells 320. For example, results of such biological tests for I7L indicate that of the 3,460 compounds identified by *in silico* screening, 136 inhibit viral replication and are not toxic. Additionally, compounds may be evaluated to determine if they inhibit enzymatic activity of the protein of interest 330. For example, for I7L, the cleavage of an I7L substrate, P4b, may be measured by electrophoresis of proteins from cell lysates from vaccinia virus-infected cells on SDS-PAGE gels. Treatment with TTP-A of viral infected cells results in inhibition of the cleavage of the P4b protein, as expected if TTP-A inhibits the catalytic activity of I7L (Byrd, C.M., et al., 2004, *J. Virol.* 78:12147-12156).

The results of the biological testing may indicate that certain structures are of interest as displaying efficacy as anti-viral agents. Thus, there is the option 399 to test at least some of these structures in additional *in silico* assays to determine if additional chemical modifications may be made to the structures to improve the therapeutic effects. Or, the compounds may then considered to be optimized, and thus, comprise lead compounds for additional animal studies and the like 400.

Therapeutics

The invention further provides pharmaceutical compositions comprising the antiviral active compounds of the invention. The pharmaceutical compositions containing a compound of the invention may be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous, or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups or elixirs. Compositions intended for oral use may be prepared according to any known method,

and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents, and preserving agents in order to provide pharmaceutically elegant and palatable preparations. Tablets may contain the active ingredient in admixture with non-toxic

5 pharmaceutically-acceptable excipients which are suitable for the manufacture of tablets. These excipients may be for example, inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, for example corn starch or alginic acid; binding agents, for example, starch, gelatin or acacia; and lubricating agents, for example

10 magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate may be employed. They may also be coated by the techniques described in U.S.

15 Patent Nos. 4,356,108; 4,166,452; and 4,265,874, to form osmotic therapeutic tablets for controlled release.

Formulations for oral use may also be presented as hard gelatin capsules where the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or a soft gelatin capsules wherein

20 the active ingredient is mixed with water or an oil medium, for example peanut oil, liquid paraffin, or olive oil.

Aqueous suspensions may contain the active compounds in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose,

25 hydroxypropylmethylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents may be a naturally-occurring phosphatide such as lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example, heptadecaethyl-eneoxycetanol,

30 or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also

contain one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose or saccharin.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active compound in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example, sweetening, flavoring, and coloring agents may also be present.

The pharmaceutical compositions of the invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, for example, olive oil or arachis oil, or a mineral oil, for example a liquid paraffin, or a mixture thereof. Suitable emulsifying agents may be naturally-occurring gums, for example gum acacia or gum tragacanth, naturally-occurring phosphatides, for example soy bean, lecithin, and esters or partial esters derived from fatty acids and hexitol anhydrides, for example sorbitan monooleate, and condensation products of said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening and flavoring agents.

Also, oily suspensions may be formulated by suspending the active ingredient in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as a liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents such as those set forth above, and flavoring agents may be added to provide a palatable oral preparation. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

Syrups and elixirs may be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative and flavoring and coloring agents.

The pharmaceutical compositions may also be in the form of a sterile injectible aqueous or oleaginous suspension. This suspension may be formulated according to the known methods using suitable dispersing or wetting agents and suspending agents described above. The sterile injectible preparation may also be a sterile injectible solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic

sodium chloride solution. In addition, sterile, fixed oils are conveniently employed as solvent or suspending medium. For this purpose, any bland fixed oil may be employed using synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectibles.

5 The compositions may also be in the form of suppositories for rectal administration of the compounds of the invention. These compositions can be prepared by mixing the drug with a suitable non-irritating excipient which is solid at ordinary temperatures but liquid at the rectal temperature and will thus melt in the rectum to release the drug. Such materials include cocoa butter and polyethylene
10 glycols, for example.

For topical use, as for example for treatment of molluscipox virus, creams, ointments, jellies, solutions of suspensions, etc., containing the compounds of the invention are contemplated. For the purpose of this application, topical applications shall include mouthwashes and gargles.

15 The compounds of the present invention may also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes may be formed from a variety of phospholipids, such as cholesterol, stearylamine, or phosphatidylcholines.

Also provided by the present invention are prodrugs of the invention.

20 Pharmaceutically acceptable salts of the compounds of the present invention, where a basic or acidic group is present in the structure, are also included within the scope of the invention. The term "pharmaceutically acceptable salts" refers to non-toxic salts of the compounds of this invention which are generally prepared by reacting the free base with a suitable organic or inorganic acid or by reacting the acid
25 with a suitable organic or inorganic base. Representative salts include the following salts: Acetate, Benzenesulfonate, Benzoate, Bicarbonate, Bisulfate, Bitartrate, Borate, Bromide, Calcium Edetate, Camsylate, Carbonate, Chloride, Clavulanate, Citrate, Dihydrochloride, Edetate, Edisylate, Estolate, Esylate, Fumarate, Gluceptate, Gluconate, Glutamate, Glycolylarsanilate, Hexylresorcinate, Hydrabamine,
30 Hydrobromide, Hydrochloride, Hydroxynaphthoate, Iodide, Isethionate, Lactate, Lactobionate, Laurate, Malate, Maleate, Mandelate, Methanesulfonate, Methylbromide, Methylnitrate, Methylsulfate, Monopotassium Maleate, Mucate, Napsylate, Nitrate, N-methylglucamine, Oxalate, Pamoate (Embonate), Palmitate, Pantothenate, Phosphate/diphosphate, Polygalacturonate, Potassium, Salicylate,

Sodium, Stearate, Subacetate, Succinate, Tannate, Tartrate, Teoclate, Tosylate, Triethiodide, Trimethylammonium and Valerate. When an acidic substituent is present, such as—COOH, there can be formed the ammonium, morpholinium, sodium, potassium, barium, calcium salt, and the like, for use as the dosage form. When a
5 basic group is present, such as amino or a basic heteroaryl radical, such as pyridyl, an acidic salt, such as hydrochloride, hydrobromide, phosphate, sulfate, trifluoroacetate, trichloroacetate, acetate, oxalate, male ate, private, malamute, succinct, citrate, tartarate, fumarate, mandelate, benzoate, cinnamate, methanesulfonate, ethanesulfonate, picrate and the like. Other salts, which are not pharmaceutically
10 acceptable, may be useful in the preparation of compounds of the invention; these form a further aspect of the invention.

In addition, some of the compounds identified as binding to, or modulating I7L, may form solvates with water or common organic solvents. Such solvates are also encompassed within the scope of the invention.

15 Thus, in another embodiment of the present invention, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound identified as binding to or modulating I7L, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, and one or more pharmaceutically acceptable carriers, excipients, or diluents. In an embodiment of the pharmaceutical
20 composition, the compound identified as binding to or modulating I7L, is an inhibitor of orthopox viruses, including smallpox virus.

In another embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of the compound identified as binding to or modulating I7L, and one or more pharmaceutically
25 acceptable carriers, excipients, or diluents, wherein said pharmaceutical composition is used to replace or supplement compounds that posses antiviral activity.

In another embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of the compound identified as binding to, or modulating I7L, and one or more pharmaceutically
30 acceptable carriers, excipients, or diluents, and further comprising one or more additional therapeutic agents.

The compound identified as binding to, or modulating I7L, may administered in an amount sufficient to reduce the viral load in a subject. The compound identified as binding to, or modulating I7L, may be administered in the form of an oral dosage

or parenteral dosage unit. In alternative embodiments, the compound identified as binding to, or modulating I7L, is administered as a dose in a range from about 0.01 to 1,000 mg/kg of body weight per day, or as a dose in a range from about 0.1 to 100 mg/kg of body weight per day, or as a dose in a range from about 0.5 to 10 mg/kg of body weight per day. In another embodiment, the compound identified as binding to, or modulating I7L, is used to replace or supplement a compound that inhibits viruses.

The present invention also provides a prophylactic method for the inhibition of pox virus infection comprising administering to a subject in need thereof a compound identified as binding to, or modulating I7L, wherein the compound is administered to the subject as a pharmaceutical composition comprising a therapeutically effective amount of the compound and one or more pharmaceutically acceptable carriers, excipients, or diluents. The therapeutically effective amount of the compound identified as binding to, or modulating I7L may inhibit a pox virus. A therapeutically effective amount of the compound identified as binding to, or modulating I7L, may comprises an amount sufficient to achieve and maintain a sustained blood level that at least partially inhibit virus growth. In alternative embodiments, the sustained blood level of the compound identified as modulating I7L may comprise a concentration ranging from about 0.01 μ M to 2 mM, or from about 1 μ M to 300 μ M, or from about 20 μ M to about 100 μ M. In another embodiment of the method, the pharmaceutical composition may further comprise one or more additional therapeutic agents.

The following is a non-exhaustive listing of adjuvants and additional therapeutic agents which may be utilized in combination with the Smallpox inhibitor of the present invention:

1. Analgesics: Aspirin
- 25 2. NSAIDs (Nonsteroidal anti-inflammatory drugs): Ibuprofen, Naproxen, Diclofenac
3. DMARDs (Disease-Modifying Antirheumatic drugs): Methotrexate, gold preparations, hydroxychloroquine, sulfasalazine
- 30 4. Biological Response Modifiers: Etanercept, Infliximab, Glucocorticoids

In a further preferred embodiment, the present invention provides a method of treating or preventing viral - mediated diseases, the method comprising administering to a subject in need thereof, a therapeutically effective amount of a compound

identified as binding to, or modulating I7L, alone or in combination with therapeutic agents selected from the group consisting of antibiotics, hormones, biologic response modifiers, analgesics, NSAIDs, DMARDs, or biological response modifiers. In one embodiment, the viral disease is caused by an orthopox virus, such as smallpox or other orthopox viruses.

For treatment of orthopox-mediated disease, or other viral disease, the compound identified as binding to, or modulating I7L, may be administered at a dosage level of from about 0.01 to 1000 mg/kg of the body weight of the subject being treated, or at a dosage range between 0.01 and 100 mg/kg, or at a dosage range between 0.5 to 10 mg/kg of body weight per day. The amount of active ingredient that may be combined with the carrier materials to produce a single dosage will vary depending upon the host being treated and the particular mode of administration. For example, a formulation intended for oral administration to humans may contain 1 mg to 2 grams of a compound identified as binding to, or modulating I7L, with an appropriate and convenient amount of carrier material, which may vary from about 5 to 95 percent of the total composition. Dosage unit forms may, in one embodiment, contain between from about 5 mg to about 500 mg of active ingredient. As is known in the art, the dosage may be individualized by the clinician based on the specific clinical condition of the subject being treated. Thus, it will be understood that the specific dosage level for any particular patient will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination and the severity of the particular disease undergoing therapy.

EXAMPLES

Example 1: Materials and Methods

Small organic compound stocks were prepared at a concentration of 10 mM in 100% dimethyl sulfoxide. The synthesis of TTP-A, TTP-B, and related compound is described in U.S. Patent Application 60/493,879, filed August 8, 2003 (TTP 2003-08). The disclosure of U.S. Patent Application 60/493,879, is hereby incorporated by reference in its entirety herein.

Cell lines used to measure toxicity of the compounds and antiviral effects included BSC40 cells, which are BSC1 African green monkey kidney cells adapted to grow at 40°C (Raczynski, P., et al., 1983, *Virology*, 128:458-462). The vvGFP line is

a Western Reserve vaccinia virus with GGP in the thymidine kinase (TK) locus (Byrd, C.M., et al., 2004, *J. Virol.*, 78:12147-12156).

Example 2: Computer Modeling

TransTech Pharma's Translational Technology™, described in U.S. Patent Applications 10/120,278, filed April 10, 2002, 10/410,965, filed April 10, 2003, and 10/411,568, filed April 10, 2003, each of which are incorporated by reference in their entireties, was used to model the I7L cysteine protease domain, to discover specific small molecule inhibitors, and to optimize I7L binding agents into preclinical drug candidates. TransTech Pharma's Translational Technology™ was designed and developed for rapid lead generation and optimization of drug candidates. The system consists of two subtechnologies: TTProbes™ and TTPredict™. TTProbes™ is a set of greater than 51,000 pharmacologically diverse molecules. TTPredict™ is a computer-based technology that automates high-throughput three-dimensional target model building, binding site identification, and conformational analysis. The TTPredict computer program is used to dock, score, and rank members of TTProbes set into a target binding site.

To develop putative anti-viral compounds, TTPredict™ was used to construct threading and homology models for I7L. I7L is known to be a member of the cysteine protease super-family and has 423 amino acid residues. Sequence comparison to proteins with experimentally determined three-dimensional (3D) structures showed that the highest sequence identity with vaccinia virus I7L is achieved by the Ubiquitin-like protease 1 (ULP1) protease C-terminal domain (PDB code:1EUV). Such sequence comparisons were performed using PDBBlast (available on-line at the NCBI web-site), 3DPSM (Bates, P.A., et al., 2001, Enhancement of Protein Modeling by Human Intervention in Applying the Automatic Programs 3D-JIGSAW and 3D-PSSM, *Proteins: Structure, Function and Genetics*, Suppl 5:39-46), MOE (MOE, Chemical Computing Group) (available on-line at the Chemical Computing Group web-site) and SeqFold within the MSI suite of programs (Accelrys Inc., San Diego, CA). ULP1 is also a member of the cysteine protease super-family and has 221 amino acids in the catalytic domain. Based on the sequence comparison, it was determined that ULP1 has a 22% sequence identity with I7L. The 303-residue ligand binding domain of I7L sequence (amino acids 110-423) was mapped onto 301 residues from the C-terminus of ULP1 protease domain using 3DPSM and the Homology modeling suites within the Accelrys suite of programs (San Diego, CA).

The sequence of the I7L polypeptide comprising the three-dimensional model of Table 2 s provided herein as SEQ ID NO. 1. Despite having only a 22% sequence identity with I7L, the 3D structure of ULP1 was successfully used as a threading template to generate a 3D model for the I7L query sequence.

5 I7L and ULP1 sequences were aligned in a manner that maintains perfect alignment of their conserved residues. In particular, their catalytic Cys – His – Trp combination from the ULP1 catalytic domain were used as hang points to anchor I7L sequence on the 3D structure of ULP1. The threading protocols identified a Cys/His/Trp hang points triplets in I7L to be residues His241/Cys328/Trp168. The
10 corresponding triplets in ULP1 protease were identified to be His514/Cys580/Trp448. Following threading, the C α atoms of I7L residues were placed at the corresponding C α positions of ULP1 using Homology module (Accelrys, San Diego, CA). The resulting structure was energy minimized using Discover (Accelrys) to generate I7L structure that served as a model. The hang point residues are shown in FIG. 1, which
15 also shows the locations of these residues in I7L and ULP1 protease.

Site search algorithms were used to identify the catalytic site of I7L. The resulting model agrees well with previous structural and biochemical studies for cysteine proteases. For example, several conserved amino acids including His241, Trp242, Asp248, Asp258, Gln322, Cys328, and Gly329, have been experimentally
20 shown to be relevant for I7L catalytic activity. In the three-dimensional model generated for I7L, it was found that most of these residues are located in the immediate vicinity of the catalytic site (FIG. 2).

Table 2 provides the coordinates for the three dimensional structure for I7L developed using the methods of the present invention. In this table, from the left, the
25 second column identifies atom number; the third identifies atom type; the fourth column identifies amino acid type; the fifth column identifies the residue number; the sixth column identifies the x coordinates, the seventh column identifies y coordinates; and the eighth column identifies the z coordinates. Also, shown in the ninth column the occupancy, and the last column of Table 2 provides the temperature factor or B
30 factor. The B factor can be defined as:

$$B=8* \pi^2 (<u^2> + <u^2>);$$

where $<u^2>$, is the dynamic variability, and contains information on atom variability in an exposed versus buried state, and the temperature dependence on variation; and

<us2>, is the static variability, and contains information relating to unresolved occupancy, altered electron density, and crystal disorder. The occupancy and B factor fields are not required for the analyses described herein, however.

Example 3 In Silico Assay

5 TTProbes were docked into the ligand binding site (FIG. 3). The fit of every docked probe was computed using several scoring functions. High-scoring probes were identified, and the highest ranking TTProbes were submitted for *in vivo* screening.

For I7L, the amino acid residues His 241, Trp 242, Asp 248, Asp 258, Gln
10 322, Cys 328, Gly 329, Leu324, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Met195, Ser326, Glu327, Leu239, Leu177, and/or Met233 are predicted to be important in binding to substrates. In Table 1, additional amino acid residues that potentially bind to the substrate protein as well as that can bind to small molecule ligands are listed. Amino acids shown in bold font in the Table 1 are residues that
15 appear to be critical in binding to small molecule ligands. Amino acid residues that are not in bold also constitute the ligand binding site. For clarity, only a few amino acid residues are identified in FIGS. 1-5, which show the ligand binding site.

The 51,389 probe molecules comprising TTProbesTM database were then docked into the catalytic site. The fit of every docked probe was computed using
20 several scoring functions. Prior to docking the probes into I7L active site, 1000 low energy conformers per probe were generated using Monte-Carlo procedures. TTPredictTM was used to dock *in silico* every conformer into the predicted site of I7L. Individual or consensus scoring functions including LUDI (Böhm, H.J., 1994, *J. Comp. Aided Molec. Design*, 8:243-256), PLP (Gehlhaar et al, 1995, *Chem. Bio.*,
25 2:317-324), DOCK (Meng, E.C., et al., 1992, *J. Comp. Chem.* 13:505-524), LigFit, (Accelrys, San Diego, CA), JAIN (Jain, A.N., 1996, *J. Comp. Aided Molec. Design* 10:427-440), and Poisson-Boltzmann (Honig, B. et al., 1995, *Science*, 268:1144-9) were used. High consensus scoring probes were identified and the 3,480 highest-ranking probes were submitted for *in vitro* (i.e., biological) testing. This process led
30 to the identification of several lead compounds including, but not limited to, TTP-A and TTP-B.

Tables 3 and 4 provide the coordinates for the computed low-energy docking modes for TTP-A and TTP-B, respectively. Thus, the three-dimensional coordinates as listed in Tables 3 and 4 provide structures for TTP-A and TTP-B as each

compound interacts with I7L. The docking modes as provided in Tables 2 and 3 are presented in order of increasing energy, where a low energy associated with docking the compound into the I7L protein is thermodynamically more favorable than a high energy of interaction. The low-energy docking modes for TTP-A and TTP-B as shown in Tables 3 and 4 favor interactions with I7L residues listed in Table 1. In Tables 3 and 4, from the left, the second column identifies atom number, the third column identifies atom type, the fourth column identifies molecule name, the sixth column identifies the x coordinates, the seventh column identifies y coordinates and the eighth column identifies the z coordinates. The last column of Tables 3 and 4 provides the temperature (B) factor.

Biological Assay

The following assay methods may be utilized to identify compounds that are effective in showing antiviral activity against vaccinia virus.

a. Cytotoxicity Assay

Cytopathic effect was measured on the BSC40 african green monkey kidney cells using 100 μ M concentrations of the compounds tested in silico. In this assay, 96-well black Packard viewplates were seeded with BSC40 cells (2.25×10^4 cells/well) in Minimum Essential Media supplemented with 5% FCS, 2mM L-glutamine and 10 μ g/mL gentamycin sulfate. When the cells became confluent (24 hrs) they were treated with 100 μ M compound diluted in media. The cells were placed in an incubator at 37°C (5% CO₂) for 24 hours, and checked for toxicity via direct observation under the microscope and also with alamar blue which assesses cell viability and proliferation (healthy cells produce a visible color change from blue to red). The cells were scored on a scale of 0-3 where 0 corresponds to normal healthy cells, 1 corresponds to unhealthy cells but not rounding up, 2 corresponds to cells that are rounding up, and 3 corresponds to cells that have rounded up and pulled off the plate. Compounds at concentrations that scored 1 or greater were diluted and the above assay was repeated to find the concentration at which the compound scored 0.

It was found that TTP-A exhibited a TC50 value of about 900 μ M, and TTP-B exhibited a TC50 value of about 600 μ M.

b. Anti-viral assay

A vvGFP assay may be performed to test the ability of each compound to inhibit viral growth as measured by a reduction in fluorescence from vaccinia virus

expressing the green fluorescent protein (vvGFP). In this assay, 96-well black Packard viewplates are seeded with BSC40 cells in Minimum Essential Media supplemented with 5% FCS, 2mM L-glutamine, and 10 µg/mL gentamycin sulfate. When the cells are confluent they are washed with PBS and then infected with vaccinia virus at a multiplicity of infection (MOI) of 0.1 for 30 min in PBS. At 30 minutes, the cells are overlaid with 100 µl of infection media supplemented with the compound of interest in doubling dilutions. As controls, infected cells are treated with rifampicin (to block assembly of DNA and protein into mature virus particles), AraC, hydroxyurea, with no compound, or mock infected. Cells are put in a 37°C incubator (5% CO₂) for 24 hrs. At 24 hours post infection (pi), the plates are removed from the incubator, washed with PBS and fluorescence measured on a Wallac plate reader (using an excitation of 485 nm and reading at 535 nm). Wells that show reduced fluorescence are checked visually under the microscope to verify a reduction in viral infection versus a loss of cells due to cytopathic effect from virus infection. Compounds that are found to inhibit viral replication are then checked for inhibitory effect at various concentrations to determine the IC₅₀ and the therapeutic index. It was found that TTP-A exhibited a IC₅₀ value of about 12 µM, and TTP-B exhibited a IC₅₀ value of about 4.6 µM.

c. Determination of TI

The 50% inhibitor concentrations (IC₅₀) were determined by cytopathic effect (CPE) inhibition as seen by fluorescence using vvGFP and plaque reduction assays with crystal violet staining or neutral red uptake. The 50% cell toxicity concentration (TC₅₀) were determined as the concentrations of compounds that caused 50% of the cells to round up and show signs of toxicity both visibly and by the Alamar Blue dye assay. The therapeutic index was calculated as the value for TC₅₀ divided by IC₅₀. For TTP-A, a TI of about 75 was calculated. For TTP-B, a TI of about 130 was calculated.

Example 3: Drug-Resistant Viruses

To demonstrate that the target of TTP-A mediated inhibition is I7L protein, vvGFP was subjected to numerous passages in the presence of TTP-A to generate drug-resistant viral mutants (Byrd, C.M., et al., 2004, *J. Virol.* 78:12147-12156). Cells were infected with vvGFP at an MOI of 0.1 in the presence of the IC₅₀ concentration of TTP-A for 24 h prior to being harvested. After determining the

titer, a portion of the virus-infected cell extract was used to infect fresh BSC40 cells. The titer of virus dropped seven logs from passage 0 to 4. Starting with passage 5, the progeny titer began to rise in the presence of the drug until a four log increase was observed by passage 7, presumably due to the emergence of a drug-resistant mutant population. After passage 9, individual viral plaques were purified, and the viral DNA isolated and sequenced. All of the resistant viruses were found to have mutations in positions 104 and 324, with a Y to C mutation at 104, and an L to M mutation at 324. FIG. 5 shows a model of the I7L active site showing the position of Leu324 in close proximity to the catalytic cysteine, Cys328.

While the invention has been described and illustrated with reference to certain preferred embodiments thereof, those skilled in the art will appreciate that various changes, modifications and substitutions can be made therein without departing from the spirit and scope of the invention. For example, effective dosages other than the preferred dosages as set forth herein may be applicable as a consequence of variations in the responsiveness of the mammal being treated for orthopox-mediated disease(s). Likewise, the specific pharmacological responses observed may vary according to and depending on the particular active compound selected or whether there are present pharmaceutical carriers, as well as the type of formulation and mode of administration employed, and such expected variations or differences in the results are contemplated in accordance with the objects and practices of the present invention.

TABLE -2

REMARK Model of I7L cysteine protease domain

REMARK									
ATOM	1	N	LYS	120	35.399	18.046	91.616	1.00	33.54
ATOM	2	CA	LYS	120	36.155	19.054	90.839	1.00	33.54
ATOM	3	CB	LYS	120	36.788	18.386	89.607	1.00	33.54
ATOM	4	CG	LYS	120	37.840	17.338	89.979	1.00	33.54
ATOM	5	CD	LYS	120	38.181	16.372	88.842	1.00	33.54
ATOM	6	CE	LYS	120	39.240	15.329	89.215	1.00	33.54
ATOM	7	NZ	LYS	120	39.370	14.324	88.133	1.00	33.54
ATOM	8	C	LYS	120	35.214	20.123	90.391	1.00	33.54
ATOM	9	O	LYS	120	34.007	19.904	90.314	1.00	33.54
ATOM	10	N	PRO	121	35.732	21.292	90.132	1.00	130.82
ATOM	11	CA	PRO	121	34.868	22.345	89.684	1.00	130.82
ATOM	12	CD	PRO	121	36.861	21.796	90.893	1.00	130.82
ATOM	13	CB	PRO	121	35.646	23.643	89.883	1.00	130.82
ATOM	14	CG	PRO	121	36.621	23.308	91.027	1.00	130.82
ATOM	15	C	PRO	121	34.458	22.088	88.276	1.00	130.82
ATOM	16	O	PRO	121	35.303	21.715	87.465	1.00	130.82
ATOM	17	N	ARG	122	33.164	22.271	87.970	1.00	108.62
ATOM	18	CA	ARG	122	32.676	22.105	86.635	1.00	108.62
ATOM	19	CB	ARG	122	31.139	22.137	86.561	1.00	108.62
ATOM	20	CG	ARG	122	30.463	21.010	87.349	1.00	108.62
ATOM	21	CD	ARG	122	30.257	19.714	86.559	1.00	108.62
ATOM	22	NE	ARG	122	31.599	19.128	86.270	1.00	108.62
ATOM	23	CZ	ARG	122	32.195	19.334	85.057	1.00	108.62
ATOM	24	NH1	ARG	122	31.553	20.056	84.094	1.00	108.62
ATOM	25	NH2	ARG	122	33.429	18.808	84.806	1.00	108.62
ATOM	26	C	ARG	122	33.186	23.250	85.820	1.00	108.62
ATOM	27	O	ARG	122	33.508	23.103	84.643	1.00	108.62
ATOM	28	N	LEU	123	33.260	24.433	86.458	1.00	72.61
ATOM	29	CA	LEU	123	33.634	25.666	85.824	1.00	72.61
ATOM	30	CB	LEU	123	33.074	26.863	86.591	1.00	72.61
ATOM	31	CG	LEU	123	33.617	28.215	86.135	1.00	72.61
ATOM	32	CD2	LEU	123	33.353	29.259	87.223	1.00	72.61
ATOM	33	CD1	LEU	123	33.125	28.598	84.735	1.00	72.61
ATOM	34	C	LEU	123	35.117	25.813	85.846	1.00	72.61
ATOM	35	O	LEU	123	35.709	26.039	86.898	1.00	72.61
ATOM	36	N	ARG	124	35.742	25.733	84.657	1.00	69.73
ATOM	37	CA	ARG	124	37.165	25.842	84.529	1.00	69.73
ATOM	38	CB	ARG	124	37.696	25.293	83.192	1.00	69.73
ATOM	39	CG	ARG	124	37.332	23.830	82.919	1.00	69.73
ATOM	40	CD	ARG	124	37.850	23.313	81.573	1.00	69.73
ATOM	41	NE	ARG	124	37.270	21.957	81.360	1.00	69.73
ATOM	42	CZ	ARG	124	37.185	21.439	80.100	1.00	69.73
ATOM	43	NH1	ARG	124	37.678	22.141	79.037	1.00	69.73
ATOM	44	NH2	ARG	124	36.598	20.222	79.901	1.00	69.73
ATOM	45	C	ARG	124	37.513	27.293	84.548	1.00	69.73
ATOM	46	O	ARG	124	36.703	28.143	84.182	1.00	69.73
ATOM	47	N	GLU	125	38.736	27.625	85.002	1.00	99.91
ATOM	48	CA	GLU	125	39.122	28.999	84.932	1.00	99.91
ATOM	49	CB	GLU	125	39.774	29.571	86.198	1.00	99.91
ATOM	50	CG	GLU	125	41.124	28.962	86.547	1.00	99.91
ATOM	51	CD	GLU	125	41.597	29.709	87.780	1.00	99.91
ATOM	52	OE1	GLU	125	41.288	30.928	87.873	1.00	99.91
ATOM	53	OE2	GLU	125	42.257	29.078	88.646	1.00	99.91
ATOM	54	C	GLU	125	40.099	29.093	83.812	1.00	99.91
ATOM	55	O	GLU	125	40.881	28.175	83.570	1.00	99.91
ATOM	56	N	LYS	126	40.057	30.220	83.085	1.00	124.58
ATOM	57	CA	LYS	126	40.858	30.377	81.910	1.00	124.58
ATOM	58	CB	LYS	126	40.290	31.417	80.932	1.00	124.58
ATOM	59	CG	LYS	126	38.982	30.960	80.284	1.00	124.58
ATOM	60	CD	LYS	126	37.862	30.713	81.296	1.00	124.58
ATOM	61	CE	LYS	126	37.580	31.908	82.209	1.00	124.58

ATOM	62	NZ	LYS	126	36.552	31.544	83.207	1.00124.58
ATOM	63	C	LYS	126	42.249	30.784	82.254	1.00124.58
ATOM	64	O	LYS	126	42.528	31.325	83.322	1.00124.58
ATOM	65	N	VAL	127	43.162	30.486	81.309	1.00 43.57
ATOM	66	CA	VAL	127	44.543	30.843	81.385	1.00 43.57
ATOM	67	CB	VAL	127	45.391	30.078	80.411	1.00 43.57
ATOM	68	CG1	VAL	127	46.853	30.528	80.553	1.00 43.57
ATOM	69	CG2	VAL	127	45.177	28.575	80.660	1.00 43.57
ATOM	70	C	VAL	127	44.590	32.296	81.023	1.00 43.57
ATOM	71	O	VAL	127	43.634	32.836	80.472	1.00 43.57
ATOM	72	N	SER	128	45.701	32.975	81.361	1.00 27.55
ATOM	73	CA	SER	128	45.817	34.385	81.130	1.00 27.55
ATOM	74	CB	SER	128	47.193	34.936	81.534	1.00 27.55
ATOM	75	OG	SER	128	47.397	34.783	82.931	1.00 27.55
ATOM	76	C	SER	128	45.641	34.676	79.673	1.00 27.55
ATOM	77	O	SER	128	44.968	35.638	79.309	1.00 27.55
ATOM	78	N	LYS	129	46.229	33.845	78.792	1.00 93.74
ATOM	79	CA	LYS	129	46.155	34.125	77.387	1.00 93.74
ATOM	80	CB	LYS	129	46.873	33.071	76.522	1.00 93.74
ATOM	81	CG	LYS	129	46.278	31.664	76.647	1.00 93.74
ATOM	82	CD	LYS	129	46.694	30.709	75.522	1.00 93.74
ATOM	83	CE	LYS	129	46.082	29.310	75.632	1.00 93.74
ATOM	84	NZ	LYS	129	46.523	28.653	76.883	1.00 93.74
ATOM	85	C	LYS	129	44.722	34.126	76.961	1.00 93.74
ATOM	86	O	LYS	129	44.268	35.036	76.268	1.00 93.74
ATOM	87	N	ALA	130	43.965	33.103	77.394	1.00 27.03
ATOM	88	CA	ALA	130	42.599	32.952	76.991	1.00 27.03
ATOM	89	CB	ALA	130	41.962	31.668	77.545	1.00 27.03
ATOM	90	C	ALA	130	41.786	34.106	77.481	1.00 27.03
ATOM	91	O	ALA	130	40.931	34.618	76.760	1.00 27.03
ATOM	92	N	ILE	131	42.031	34.550	78.728	1.00 34.84
ATOM	93	CA	ILE	131	41.253	35.613	79.303	1.00 34.84
ATOM	94	CB	ILE	131	41.617	35.916	80.726	1.00 34.84
ATOM	95	CG2	ILE	131	40.905	37.219	81.125	1.00 34.84
ATOM	96	CG1	ILE	131	41.279	34.722	81.635	1.00 34.84
ATOM	97	CD1	ILE	131	41.796	34.881	83.065	1.00 34.84
ATOM	98	C	ILE	131	41.446	36.870	78.517	1.00 34.84
ATOM	99	O	ILE	131	40.492	37.605	78.266	1.00 34.84
ATOM	100	N	ASP	132	42.691	37.148	78.100	1.00 68.91
ATOM	101	CA	ASP	132	42.986	38.364	77.403	1.00 68.91
ATOM	102	CB	ASP	132	44.470	38.463	77.009	1.00 68.91
ATOM	103	CG	ASP	132	44.720	39.870	76.490	1.00 68.91
ATOM	104	OD1	ASP	132	43.756	40.683	76.514	1.00 68.91
ATOM	105	OD2	ASP	132	45.872	40.152	76.063	1.00 68.91
ATOM	106	C	ASP	132	42.186	38.398	76.141	1.00 68.91
ATOM	107	O	ASP	132	41.673	39.443	75.746	1.00 68.91
ATOM	108	N	PHE	133	42.048	37.232	75.485	1.00 73.74
ATOM	109	CA	PHE	133	41.365	37.133	74.230	1.00 73.74
ATOM	110	CB	PHE	133	41.384	35.691	73.696	1.00 73.74
ATOM	111	CG	PHE	133	40.936	35.690	72.275	1.00 73.74
ATOM	112	CD1	PHE	133	41.817	36.027	71.274	1.00 73.74
ATOM	113	CD2	PHE	133	39.649	35.344	71.943	1.00 73.74
ATOM	114	CE1	PHE	133	41.416	36.025	69.958	1.00 73.74
ATOM	115	CE2	PHE	133	39.242	35.341	70.629	1.00 73.74
ATOM	116	CZ	PHE	133	40.126	35.683	69.635	1.00 73.74
ATOM	117	C	PHE	133	39.943	37.555	74.434	1.00 73.74
ATOM	118	O	PHE	133	39.386	38.308	73.634	1.00 73.74
ATOM	119	N	SER	134	39.316	37.087	75.529	1.00 70.77
ATOM	120	CA	SER	134	37.947	37.423	75.794	1.00 70.77
ATOM	121	CB	SER	134	37.418	36.775	77.085	1.00 70.77
ATOM	122	OG	SER	134	37.409	35.360	76.959	1.00 70.77
ATOM	123	C	SER	134	37.831	38.909	75.958	1.00 70.77
ATOM	124	O	SER	134	36.913	39.529	75.424	1.00 70.77
ATOM	125	N	GLN	135	38.783	39.529	76.677	1.00 36.15
ATOM	126	CA	GLN	135	38.709	40.937	76.956	1.00 36.15
ATOM	127	CB	GLN	135	39.893	41.434	77.808	1.00 36.15

ATOM	128	CG	GLN	135	39.866	42.932	78.126	1.00	36.15
ATOM	129	CD	GLN	135	38.813	43.192	79.191	1.00	36.15
ATOM	130	OE1	GLN	135	37.713	42.647	79.137	1.00	36.15
ATOM	131	NE2	GLN	135	39.162	44.045	80.192	1.00	36.15
ATOM	132	C	GLN	135	38.731	41.714	75.675	1.00	36.15
ATOM	133	O	GLN	135	37.973	42.668	75.510	1.00	36.15
ATOM	134	N	MET	136	39.596	41.316	74.724	1.00	31.95
ATOM	135	CA	MET	136	39.739	42.050	73.500	1.00	31.95
ATOM	136	CB	MET	136	40.810	41.436	72.586	1.00	31.95
ATOM	137	CG	MET	136	42.207	41.448	73.209	1.00	31.95
ATOM	138	SD	MET	136	43.465	40.522	72.280	1.00	31.95
ATOM	139	CE	MET	136	43.593	41.727	70.929	1.00	31.95
ATOM	140	C	MET	136	38.447	42.026	72.743	1.00	31.95
ATOM	141	O	MET	136	38.001	43.051	72.228	1.00	31.95
ATOM	142	N	ASP	137	37.800	40.849	72.676	1.00	41.81
ATOM	143	CA	ASP	137	36.595	40.710	71.914	1.00	41.81
ATOM	144	CB	ASP	137	36.073	39.264	71.857	1.00	41.81
ATOM	145	CG	ASP	137	36.953	38.498	70.877	1.00	41.81
ATOM	146	OD1	ASP	137	37.243	39.059	69.786	1.00	41.81
ATOM	147	OD2	ASP	137	37.336	37.341	71.198	1.00	41.81
ATOM	148	C	ASP	137	35.519	41.570	72.501	1.00	41.81
ATOM	149	O	ASP	137	34.735	42.177	71.776	1.00	41.81
ATOM	150	N	LEU	138	35.467	41.658	73.838	1.00	100.75
ATOM	151	CA	LEU	138	34.440	42.407	74.494	1.00	100.75
ATOM	152	CB	LEU	138	34.625	42.351	76.028	1.00	100.75
ATOM	153	CG	LEU	138	33.547	43.003	76.929	1.00	100.75
ATOM	154	CD2	LEU	138	33.267	44.480	76.598	1.00	100.75
ATOM	155	CD1	LEU	138	33.931	42.830	78.409	1.00	100.75
ATOM	156	C	LEU	138	34.552	43.836	74.043	1.00	100.75
ATOM	157	O	LEU	138	33.543	44.490	73.785	1.00	100.75
ATOM	158	N	LYS	139	35.786	44.362	73.951	1.00	110.99
ATOM	159	CA	LYS	139	36.007	45.744	73.630	1.00	110.99
ATOM	160	CB	LYS	139	37.415	46.265	73.985	1.00	110.99
ATOM	161	CG	LYS	139	38.580	45.713	73.166	1.00	110.99
ATOM	162	CD	LYS	139	39.861	46.515	73.415	1.00	110.99
ATOM	163	CE	LYS	139	41.113	45.959	72.734	1.00	110.99
ATOM	164	NZ	LYS	139	42.277	46.819	73.056	1.00	110.99
ATOM	165	C	LYS	139	35.696	46.112	72.205	1.00	110.99
ATOM	166	O	LYS	139	35.380	47.274	71.954	1.00	110.99
ATOM	167	N	ILE	140	35.784	45.154	71.252	1.00	182.56
ATOM	168	CA	ILE	140	35.662	45.367	69.825	1.00	182.56
ATOM	169	CB	ILE	140	35.394	44.076	69.090	1.00	182.56
ATOM	170	CG2	ILE	140	33.944	43.652	69.362	1.00	182.56
ATOM	171	CG1	ILE	140	35.744	44.188	67.600	1.00	182.56
ATOM	172	CD1	ILE	140	34.883	45.179	66.830	1.00	182.56
ATOM	173	C	ILE	140	34.591	46.380	69.511	1.00	182.56
ATOM	174	O	ILE	140	33.449	46.280	69.954	1.00	182.56
ATOM	175	N	ASP	141	34.971	47.425	68.741	1.00	152.17
ATOM	176	CA	ASP	141	34.097	48.531	68.453	1.00	152.17
ATOM	177	CB	ASP	141	34.810	49.688	67.725	1.00	152.17
ATOM	178	CG	ASP	141	33.873	50.896	67.721	1.00	152.17
ATOM	179	OD1	ASP	141	32.825	50.827	68.417	1.00	152.17
ATOM	180	OD2	ASP	141	34.188	51.898	67.025	1.00	152.17
ATOM	181	C	ASP	141	32.925	48.138	67.605	1.00	152.17
ATOM	182	O	ASP	141	31.792	48.505	67.908	1.00	152.17
ATOM	183	N	ASP	142	33.155	47.380	66.517	1.00	218.47
ATOM	184	CA	ASP	142	32.078	47.107	65.608	1.00	218.47
ATOM	185	CB	ASP	142	32.531	47.058	64.141	1.00	218.47
ATOM	186	CG	ASP	142	31.310	47.289	63.266	1.00	218.47
ATOM	187	OD1	ASP	142	30.632	48.335	63.458	1.00	218.47
ATOM	188	OD2	ASP	142	31.049	46.429	62.382	1.00	218.47
ATOM	189	C	ASP	142	31.409	45.813	65.949	1.00	218.47
ATOM	190	O	ASP	142	31.944	44.984	66.683	1.00	218.47
ATOM	191	N	LEU	143	30.195	45.611	65.401	1.00	82.28
ATOM	192	CA	LEU	143	29.456	44.420	65.681	1.00	82.28
ATOM	193	CB	LEU	143	27.940	44.671	65.688	1.00	82.28

ATOM	194	CG	LEU	143	27.528	45.802	66.656	1.00	82.28
ATOM	195	CD2	LEU	143	28.095	45.575	68.067	1.00	82.28
ATOM	196	CD1	LEU	143	26.009	46.028	66.645	1.00	82.28
ATOM	197	C	LEU	143	29.763	43.467	64.575	1.00	82.28
ATOM	198	O	LEU	143	29.085	43.442	63.548	1.00	82.28
ATOM	199	N	SER	144	30.806	42.642	64.773	1.00	84.93
ATOM	200	CA	SER	144	31.222	41.716	63.764	1.00	84.93
ATOM	201	CB	SER	144	32.744	41.714	63.557	1.00	84.93
ATOM	202	OG	SER	144	33.099	40.782	62.550	1.00	84.93
ATOM	203	C	SER	144	30.811	40.346	64.203	1.00	84.93
ATOM	204	O	SER	144	30.408	40.147	65.349	1.00	84.93
ATOM	205	N	ARG	145	30.893	39.361	63.285	1.00	99.45
ATOM	206	CA	ARG	145	30.495	38.020	63.611	1.00	99.45
ATOM	207	CB	ARG	145	29.996	37.210	62.402	1.00	99.45
ATOM	208	CG	ARG	145	31.049	37.044	61.307	1.00	99.45
ATOM	209	CD	ARG	145	30.544	36.270	60.089	1.00	99.45
ATOM	210	NE	ARG	145	31.664	36.206	59.108	1.00	99.45
ATOM	211	CZ	ARG	145	31.393	36.165	57.769	1.00	99.45
ATOM	212	NH1	ARG	145	30.102	36.187	57.332	1.00	99.45
ATOM	213	NH2	ARG	145	32.418	36.104	56.870	1.00	99.45
ATOM	214	C	ARG	145	31.681	37.305	64.173	1.00	99.45
ATOM	215	O	ARG	145	32.709	37.159	63.514	1.00	99.45
ATOM	216	N	LYS	146	31.566	36.900	65.454	1.00	170.67
ATOM	217	CA	LYS	146	32.599	36.199	66.166	1.00	170.67
ATOM	218	CB	LYS	146	32.405	36.207	67.689	1.00	170.67
ATOM	219	CG	LYS	146	33.548	35.509	68.432	1.00	170.67
ATOM	220	CD	LYS	146	34.895	36.235	68.340	1.00	170.67
ATOM	221	CE	LYS	146	35.822	35.707	67.238	1.00	170.67
ATOM	222	NZ	LYS	146	35.493	36.331	65.938	1.00	170.67
ATOM	223	C	LYS	146	32.714	34.770	65.741	1.00	170.67
ATOM	224	O	LYS	146	33.812	34.216	65.711	1.00	170.67
ATOM	225	N	GLY	147	31.578	34.107	65.446	1.00	42.81
ATOM	226	CA	GLY	147	31.717	32.728	65.079	1.00	42.81
ATOM	227	C	GLY	147	30.442	32.253	64.477	1.00	42.81
ATOM	228	O	GLY	147	29.360	32.720	64.831	1.00	42.81
ATOM	229	N	ILE	148	30.559	31.317	63.517	1.00	135.88
ATOM	230	CA	ILE	148	29.411	30.705	62.922	1.00	135.88
ATOM	231	CB	ILE	148	29.117	31.213	61.533	1.00	135.88
ATOM	232	CG2	ILE	148	30.364	31.015	60.657	1.00	135.88
ATOM	233	CG1	ILE	148	27.850	30.548	60.974	1.00	135.88
ATOM	234	CD1	ILE	148	26.568	30.951	61.702	1.00	135.88
ATOM	235	C	ILE	148	29.693	29.237	62.839	1.00	135.88
ATOM	236	O	ILE	148	30.700	28.824	62.265	1.00	135.88
ATOM	237	N	HIS	149	28.822	28.397	63.435	1.00	129.16
ATOM	238	CA	HIS	149	29.042	26.989	63.306	1.00	129.16
ATOM	239	ND1	HIS	149	31.259	24.787	62.306	1.00	129.16
ATOM	240	CG	HIS	149	30.723	25.107	63.534	1.00	129.16
ATOM	241	CB	HIS	149	30.353	26.501	63.947	1.00	129.16
ATOM	242	NE2	HIS	149	31.102	22.884	63.445	1.00	129.16
ATOM	243	CD2	HIS	149	30.633	23.933	64.217	1.00	129.16
ATOM	244	CE1	HIS	149	31.468	23.446	62.307	1.00	129.16
ATOM	245	C	HIS	149	27.912	26.272	63.973	1.00	129.16
ATOM	246	O	HIS	149	27.326	26.763	64.935	1.00	129.16
ATOM	247	N	THR	150	27.571	25.081	63.445	1.00	179.98
ATOM	248	CA	THR	150	26.541	24.248	63.993	1.00	179.98
ATOM	249	CB	THR	150	26.887	23.769	65.380	1.00	179.98
ATOM	250	OG1	THR	150	28.162	23.143	65.354	1.00	179.98
ATOM	251	CG2	THR	150	25.847	22.736	65.856	1.00	179.98
ATOM	252	C	THR	150	25.249	25.014	64.002	1.00	179.98
ATOM	253	O	THR	150	24.363	24.774	64.819	1.00	179.98
ATOM	254	N	GLY	151	25.097	25.967	63.066	1.00	40.25
ATOM	255	CA	GLY	151	23.842	26.653	62.928	1.00	40.25
ATOM	256	C	GLY	151	23.686	27.753	63.937	1.00	40.25
ATOM	257	O	GLY	151	22.580	28.261	64.119	1.00	40.25
ATOM	258	N	GLU	152	24.761	28.150	64.641	1.00	77.36
ATOM	259	CA	GLU	152	24.597	29.251	65.551	1.00	77.36

ATOM	260	CB	GLU	152	24.867	28.897	67.024	1.00	77.36
ATOM	261	CG	GLU	152	24.688	30.087	67.968	1.00	77.36
ATOM	262	CD	GLU	152	23.221	30.490	67.936	1.00	77.36
ATOM	263	OE1	GLU	152	22.411	29.729	67.341	1.00	77.36
ATOM	264	OE2	GLU	152	22.889	31.567	68.502	1.00	77.36
ATOM	265	C	GLU	152	25.591	30.299	65.157	1.00	77.36
ATOM	266	O	GLU	152	26.781	30.013	65.031	1.00	77.36
ATOM	267	N	ASN	153	25.124	31.550	64.945	1.00	91.83
ATOM	268	CA	ASN	153	26.033	32.588	64.543	1.00	91.83
ATOM	269	CB	ASN	153	25.602	33.279	63.233	1.00	91.83
ATOM	270	CG	ASN	153	26.803	33.990	62.619	1.00	91.83
ATOM	271	OD1	ASN	153	27.948	33.754	62.997	1.00	91.83
ATOM	272	ND2	ASN	153	26.539	34.882	61.626	1.00	91.83
ATOM	273	C	ASN	153	26.041	33.642	65.611	1.00	91.83
ATOM	274	O	ASN	153	25.048	34.346	65.798	1.00	91.83
ATOM	275	N	PRO	154	27.105	33.707	66.372	1.00	157.76
ATOM	276	CA	PRO	154	27.188	34.780	67.333	1.00	157.76
ATOM	277	CD	PRO	154	27.523	32.448	66.972	1.00	157.76
ATOM	278	CB	PRO	154	27.889	34.220	68.566	1.00	157.76
ATOM	279	CG	PRO	154	27.607	32.717	68.482	1.00	157.76
ATOM	280	C	PRO	154	27.835	36.021	66.801	1.00	157.76
ATOM	281	O	PRO	154	28.727	35.922	65.960	1.00	157.76
ATOM	282	N	LYS	155	27.438	37.199	67.318	1.00	104.45
ATOM	283	CA	LYS	155	28.029	38.426	66.881	1.00	104.45
ATOM	284	CB	LYS	155	27.046	39.365	66.161	1.00	104.45
ATOM	285	CG	LYS	155	27.707	40.594	65.537	1.00	104.45
ATOM	286	CD	LYS	155	26.855	41.257	64.452	1.00	104.45
ATOM	287	CE	LYS	155	26.808	40.455	63.149	1.00	104.45
ATOM	288	NZ	LYS	155	25.975	41.155	62.145	1.00	104.45
ATOM	289	C	LYS	155	28.544	39.103	68.106	1.00	104.45
ATOM	290	O	LYS	155	28.388	38.600	69.218	1.00	104.45
ATOM	291	N	VAL	156	29.200	40.260	67.927	1.00	41.94
ATOM	292	CA	VAL	156	29.761	40.976	69.035	1.00	41.94
ATOM	293	CB	VAL	156	30.480	42.221	68.612	1.00	41.94
ATOM	294	CG1	VAL	156	30.916	42.988	69.872	1.00	41.94
ATOM	295	CG2	VAL	156	31.643	41.816	67.688	1.00	41.94
ATOM	296	C	VAL	156	28.653	41.373	69.958	1.00	41.94
ATOM	297	O	VAL	156	28.822	41.350	71.176	1.00	41.94
ATOM	298	N	VAL	157	27.485	41.744	69.400	1.00	88.03
ATOM	299	CA	VAL	157	26.391	42.181	70.216	1.00	88.03
ATOM	300	CB	VAL	157	25.167	42.545	69.417	1.00	88.03
ATOM	301	CG1	VAL	157	25.470	43.799	68.581	1.00	88.03
ATOM	302	CG2	VAL	157	24.767	41.331	68.561	1.00	88.03
ATOM	303	C	VAL	157	26.013	41.083	71.161	1.00	88.03
ATOM	304	O	VAL	157	25.806	41.332	72.348	1.00	88.03
ATOM	305	N	LYS	158	25.917	39.834	70.665	1.00	119.29
ATOM	306	CA	LYS	158	25.521	38.739	71.508	1.00	119.29
ATOM	307	CB	LYS	158	25.321	37.413	70.741	1.00	119.29
ATOM	308	CG	LYS	158	26.593	36.599	70.458	1.00	119.29
ATOM	309	CD	LYS	158	27.086	35.767	71.651	1.00	119.29
ATOM	310	CE	LYS	158	28.435	35.080	71.430	1.00	119.29
ATOM	311	NZ	LYS	158	28.872	34.421	72.683	1.00	119.29
ATOM	312	C	LYS	158	26.581	38.514	72.542	1.00	119.29
ATOM	313	O	LYS	158	26.291	38.253	73.708	1.00	119.29
ATOM	314	N	MET	159	27.851	38.634	72.120	1.00	113.21
ATOM	315	CA	MET	159	29.002	38.350	72.933	1.00	113.21
ATOM	316	CB	MET	159	30.299	38.614	72.151	1.00	113.21
ATOM	317	CG	MET	159	31.591	38.338	72.916	1.00	113.21
ATOM	318	SD	MET	159	31.999	36.577	73.119	1.00	113.21
ATOM	319	CE	MET	159	33.744	36.913	73.488	1.00	113.21
ATOM	320	C	MET	159	29.017	39.259	74.127	1.00	113.21
ATOM	321	O	MET	159	29.371	38.840	75.228	1.00	113.21
ATOM	322	N	LYS	160	28.612	40.527	73.928	1.00	132.62
ATOM	323	CA	LYS	160	28.633	41.576	74.914	1.00	132.62
ATOM	324	CB	LYS	160	28.228	42.940	74.336	1.00	132.62
ATOM	325	CG	LYS	160	28.501	44.097	75.296	1.00	132.62

ATOM	326	CD	LYS	160	28.568	45.457	74.602	1.00132.62
ATOM	327	CE	LYS	160	29.870	45.660	73.822	1.00132.62
ATOM	328	NZ	LYS	160	29.891	47.006	73.208	1.00132.62
ATOM	329	C	LYS	160	27.727	41.236	76.058	1.00132.62
ATOM	330	O	LYS	160	27.816	41.824	77.136	1.00132.62
ATOM	331	N	ILE	161	26.778	40.318	75.834	1.00105.62
ATOM	332	CA	ILE	161	25.916	39.853	76.882	1.00105.62
ATOM	333	CB	ILE	161	24.969	38.804	76.397	1.00105.62
ATOM	334	CG2	ILE	161	24.558	37.977	77.615	1.00105.62
ATOM	335	CG1	ILE	161	23.824	39.418	75.571	1.00105.62
ATOM	336	CD1	ILE	161	24.275	40.036	74.249	1.00105.62
ATOM	337	C	ILE	161	26.761	39.222	77.955	1.00105.62
ATOM	338	O	ILE	161	26.429	39.283	79.139	1.00105.62
ATOM	339	N	GLU	162	27.855	38.558	77.539	1.00101.65
ATOM	340	CA	GLU	162	28.791	37.835	78.359	1.00101.65
ATOM	341	CB	GLU	162	29.857	37.115	77.510	1.00101.65
ATOM	342	CG	GLU	162	29.289	36.055	76.558	1.00101.65
ATOM	343	CD	GLU	162	29.022	34.784	77.353	1.00101.65
ATOM	344	OE1	GLU	162	29.807	34.514	78.300	1.00101.65
ATOM	345	OE2	GLU	162	28.039	34.066	77.023	1.00101.65
ATOM	346	C	GLU	162	29.520	38.760	79.301	1.00101.65
ATOM	347	O	GLU	162	29.975	38.315	80.349	1.00101.65
ATOM	348	N	PRO	163	29.709	40.011	78.991	1.00149.57
ATOM	349	CA	PRO	163	30.404	40.832	79.941	1.00149.57
ATOM	350	CD	PRO	163	30.143	40.348	77.648	1.00149.57
ATOM	351	CB	PRO	163	30.630	42.156	79.228	1.00149.57
ATOM	352	CG	PRO	163	30.900	41.687	77.784	1.00149.57
ATOM	353	C	PRO	163	29.814	40.854	81.316	1.00149.57
ATOM	354	O	PRO	163	28.611	40.645	81.486	1.00149.57
ATOM	355	N	GLU	164	30.698	41.075	82.303	1.00109.34
ATOM	356	CA	GLU	164	30.451	40.875	83.697	1.00109.34
ATOM	357	CB	GLU	164	31.718	40.952	84.578	1.00109.34
ATOM	358	CG	GLU	164	32.595	39.692	84.553	1.00109.34
ATOM	359	CD	GLU	164	33.467	39.667	83.299	1.00109.34
ATOM	360	OE1	GLU	164	32.901	39.676	82.174	1.00109.34
ATOM	361	OE2	GLU	164	34.716	39.620	83.456	1.00109.34
ATOM	362	C	GLU	164	29.426	41.788	84.262	1.00109.34
ATOM	363	O	GLU	164	28.911	42.701	83.621	1.00109.34
ATOM	364	N	ARG	165	29.114	41.483	85.534	1.00129.57
ATOM	365	CA	ARG	165	28.160	42.146	86.357	1.00129.57
ATOM	366	CB	ARG	165	28.490	43.624	86.611	1.00129.57
ATOM	367	CG	ARG	165	29.804	43.774	87.382	1.00129.57
ATOM	368	CD	ARG	165	29.823	44.959	88.349	1.00129.57
ATOM	369	NE	ARG	165	29.072	44.525	89.562	1.00129.57
ATOM	370	CZ	ARG	165	27.712	44.640	89.597	1.00129.57
ATOM	371	NH1	ARG	165	27.046	45.184	88.536	1.00129.57
ATOM	372	NH2	ARG	165	27.012	44.212	90.687	1.00129.57
ATOM	373	C	ARG	165	26.770	41.983	85.845	1.00129.57
ATOM	374	O	ARG	165	25.997	42.935	85.757	1.00129.57
ATOM	375	N	GLY	166	26.427	40.733	85.489	1.00 25.71
ATOM	376	CA	GLY	166	25.066	40.405	85.201	1.00 25.71
ATOM	377	C	GLY	166	24.588	41.029	83.939	1.00 25.71
ATOM	378	O	GLY	166	23.469	41.537	83.889	1.00 25.71
ATOM	379	N	ALA	167	25.412	41.045	82.881	1.00 39.89
ATOM	380	CA	ALA	167	24.824	41.529	81.673	1.00 39.89
ATOM	381	CB	ALA	167	25.803	41.591	80.487	1.00 39.89
ATOM	382	C	ALA	167	23.765	40.517	81.363	1.00 39.89
ATOM	383	O	ALA	167	23.952	39.327	81.613	1.00 39.89
ATOM	384	N	TRP	168	22.604	40.959	80.841	1.00 48.42
ATOM	385	CA	TRP	168	21.553	40.012	80.588	1.00 48.42
ATOM	386	CB	TRP	168	20.214	40.650	80.184	1.00 48.42
ATOM	387	CG	TRP	168	19.480	41.360	81.299	1.00 48.42
ATOM	388	CD2	TRP	168	18.264	42.095	81.105	1.00 48.42
ATOM	389	CD1	TRP	168	19.780	41.444	82.626	1.00 48.42
ATOM	390	NE1	TRP	168	18.822	42.187	83.277	1.00 48.42
ATOM	391	CE2	TRP	168	17.882	42.594	82.351	1.00 48.42

ATOM	392	CE3	TRP	168	17.522	42.337	79.985	1.00	48.42
ATOM	393	CZ2	TRP	168	16.750	43.344	82.495	1.00	48.42
ATOM	394	CZ3	TRP	168	16.382	43.094	80.130	1.00	48.42
ATOM	395	CH2	TRP	168	16.003	43.586	81.360	1.00	48.42
ATOM	396	C	TRP	168	21.969	39.125	79.464	1.00	48.42
ATOM	397	O	TRP	168	22.502	39.585	78.456	1.00	48.42
ATOM	398	N	MET	169	21.721	37.810	79.626	1.00	113.87
ATOM	399	CA	MET	169	22.065	36.831	78.636	1.00	113.87
ATOM	400	CB	MET	169	22.066	35.398	79.189	1.00	113.87
ATOM	401	CG	MET	169	22.977	35.218	80.403	1.00	113.87
ATOM	402	SD	MET	169	24.741	35.504	80.082	1.00	113.87
ATOM	403	CE	MET	169	25.237	35.178	81.797	1.00	113.87
ATOM	404	C	MET	169	21.021	36.871	77.569	1.00	113.87
ATOM	405	O	MET	169	19.835	37.019	77.859	1.00	113.87
ATOM	406	N	SER	170	21.449	36.761	76.295	1.00	44.41
ATOM	407	CA	SER	170	20.522	36.747	75.200	1.00	44.41
ATOM	408	CB	SER	170	21.047	37.460	73.941	1.00	44.41
ATOM	409	OG	SER	170	22.180	36.772	73.432	1.00	44.41
ATOM	410	C	SER	170	20.251	35.320	74.832	1.00	44.41
ATOM	411	O	SER	170	20.873	34.395	75.353	1.00	44.41
ATOM	412	N	ASN	171	19.296	35.114	73.904	1.00	104.44
ATOM	413	CA	ASN	171	18.893	33.808	73.463	1.00	104.44
ATOM	414	CB	ASN	171	17.732	33.848	72.457	1.00	104.44
ATOM	415	CG	ASN	171	18.016	34.953	71.455	1.00	104.44
ATOM	416	OD1	ASN	171	19.150	35.139	71.017	1.00	104.44
ATOM	417	ND2	ASN	171	16.954	35.717	71.085	1.00	104.44
ATOM	418	C	ASN	171	20.036	33.154	72.758	1.00	104.44
ATOM	419	O	ASN	171	20.234	31.946	72.869	1.00	104.44
ATOM	420	N	ARG	172	20.813	33.945	71.997	1.00	54.25
ATOM	421	CA	ARG	172	21.870	33.392	71.204	1.00	54.25
ATOM	422	CB	ARG	172	22.516	34.441	70.288	1.00	54.25
ATOM	423	CG	ARG	172	21.483	35.000	69.305	1.00	54.25
ATOM	424	CD	ARG	172	22.058	35.740	68.098	1.00	54.25
ATOM	425	NE	ARG	172	20.902	36.112	67.233	1.00	54.25
ATOM	426	CZ	ARG	172	20.306	35.165	66.448	1.00	54.25
ATOM	427	NH1	ARG	172	20.754	33.875	66.474	1.00	54.25
ATOM	428	NH2	ARG	172	19.258	35.503	65.644	1.00	54.25
ATOM	429	C	ARG	172	22.901	32.758	72.085	1.00	54.25
ATOM	430	O	ARG	172	23.403	31.678	71.777	1.00	54.25
ATOM	431	N	SER	173	23.249	33.407	73.210	1.00	73.33
ATOM	432	CA	SER	173	24.218	32.835	74.104	1.00	73.33
ATOM	433	CB	SER	173	24.556	33.763	75.282	1.00	73.33
ATOM	434	OG	SER	173	25.518	33.149	76.127	1.00	73.33
ATOM	435	C	SER	173	23.647	31.573	74.677	1.00	73.33
ATOM	436	O	SER	173	24.340	30.566	74.810	1.00	73.33
ATOM	437	N	ILE	174	22.348	31.586	75.014	1.00	96.15
ATOM	438	CA	ILE	174	21.744	30.433	75.614	1.00	96.15
ATOM	439	CB	ILE	174	20.293	30.641	75.937	1.00	96.15
ATOM	440	CG2	ILE	174	19.735	29.300	76.446	1.00	96.15
ATOM	441	CG1	ILE	174	20.120	31.803	76.930	1.00	96.15
ATOM	442	CD1	ILE	174	20.838	31.583	78.260	1.00	96.15
ATOM	443	C	ILE	174	21.819	29.293	74.642	1.00	96.15
ATOM	444	O	ILE	174	22.172	28.176	75.017	1.00	96.15
ATOM	445	N	LYS	175	21.501	29.548	73.356	1.00	57.53
ATOM	446	CA	LYS	175	21.513	28.498	72.378	1.00	57.53
ATOM	447	CB	LYS	175	21.072	28.944	70.974	1.00	57.53
ATOM	448	CG	LYS	175	21.119	27.794	69.964	1.00	57.53
ATOM	449	CD	LYS	175	21.869	26.552	70.448	1.00	57.53
ATOM	450	CE	LYS	175	23.357	26.545	70.092	1.00	57.53
ATOM	451	NZ	LYS	175	23.651	25.411	69.188	1.00	57.53
ATOM	452	C	LYS	175	22.897	27.961	72.228	1.00	57.53
ATOM	453	O	LYS	175	23.090	26.751	72.121	1.00	57.53
ATOM	454	N	ASN	176	23.906	28.846	72.220	1.00	42.26
ATOM	455	CA	ASN	176	25.247	28.390	71.997	1.00	42.26
ATOM	456	CB	ASN	176	26.279	29.530	72.010	1.00	42.26
ATOM	457	CG	ASN	176	27.581	28.964	71.463	1.00	42.26

ATOM	458	OD1	ASN	176	27.661	27.787	71.116	1.00	42.26
ATOM	459	ND2	ASN	176	28.637	29.819	71.389	1.00	42.26
ATOM	460	C	ASN	176	25.631	27.426	73.082	1.00	42.26
ATOM	461	O	ASN	176	26.225	26.382	72.812	1.00	42.26
ATOM	462	N	LEU	177	25.284	27.734	74.347	1.00	56.01
ATOM	463	CA	LEU	177	25.700	26.878	75.425	1.00	56.01
ATOM	464	CB	LEU	177	25.388	27.413	76.828	1.00	56.01
ATOM	465	CG	LEU	177	25.909	26.443	77.900	1.00	56.01
ATOM	466	CD2	LEU	177	25.411	26.827	79.292	1.00	56.01
ATOM	467	CD1	LEU	177	27.438	26.312	77.835	1.00	56.01
ATOM	468	C	LEU	177	25.025	25.556	75.293	1.00	56.01
ATOM	469	O	LEU	177	25.602	24.514	75.597	1.00	56.01
ATOM	470	N	VAL	178	23.765	25.580	74.838	1.00	56.57
ATOM	471	CA	VAL	178	22.968	24.413	74.640	1.00	56.57
ATOM	472	CB	VAL	178	21.687	24.840	73.994	1.00	56.57
ATOM	473	CG1	VAL	178	20.954	23.617	73.470	1.00	56.57
ATOM	474	CG2	VAL	178	20.889	25.678	75.004	1.00	56.57
ATOM	475	C	VAL	178	23.698	23.504	73.693	1.00	56.57
ATOM	476	O	VAL	178	23.829	22.308	73.952	1.00	56.57
ATOM	477	N	SER	179	24.213	24.056	72.576	1.00	79.14
ATOM	478	CA	SER	179	24.884	23.265	71.579	1.00	79.14
ATOM	479	CB	SER	179	25.288	24.075	70.334	1.00	79.14
ATOM	480	OG	SER	179	26.339	24.971	70.655	1.00	79.14
ATOM	481	C	SER	179	26.145	22.690	72.144	1.00	79.14
ATOM	482	O	SER	179	26.496	21.546	71.857	1.00	79.14
ATOM	483	N	GLN	180	26.859	23.474	72.974	1.00	128.89
ATOM	484	CA	GLN	180	28.111	23.039	73.526	1.00	128.89
ATOM	485	CB	GLN	180	28.745	24.099	74.447	1.00	128.89
ATOM	486	CG	GLN	180	29.169	25.386	73.735	1.00	128.89
ATOM	487	CD	GLN	180	30.494	25.121	73.032	1.00	128.89
ATOM	488	OE1	GLN	180	30.978	23.992	73.010	1.00	128.89
ATOM	489	NE2	GLN	180	31.101	26.189	72.447	1.00	128.89
ATOM	490	C	GLN	180	27.867	21.823	74.360	1.00	128.89
ATOM	491	O	GLN	180	28.607	20.843	74.288	1.00	128.89
ATOM	492	N	PHE	181	26.799	21.854	75.174	1.00	112.00
ATOM	493	CA	PHE	181	26.451	20.747	76.010	1.00	112.00
ATOM	494	CB	PHE	181	25.231	21.043	76.887	1.00	112.00
ATOM	495	CG	PHE	181	24.572	19.737	77.130	1.00	112.00
ATOM	496	CD1	PHE	181	25.152	18.758	77.896	1.00	112.00
ATOM	497	CD2	PHE	181	23.344	19.500	76.566	1.00	112.00
ATOM	498	CE1	PHE	181	24.492	17.569	78.089	1.00	112.00
ATOM	499	CE2	PHE	181	22.679	18.317	76.763	1.00	112.00
ATOM	500	CZ	PHE	181	23.259	17.344	77.532	1.00	112.00
ATOM	501	C	PHE	181	26.130	19.562	75.167	1.00	112.00
ATOM	502	O	PHE	181	26.570	18.450	75.454	1.00	112.00
ATOM	503	N	ALA	182	25.356	19.768	74.092	1.00	29.66
ATOM	504	CA	ALA	182	24.965	18.663	73.275	1.00	29.66
ATOM	505	CB	ALA	182	24.070	19.093	72.100	1.00	29.66
ATOM	506	C	ALA	182	26.192	18.038	72.700	1.00	29.66
ATOM	507	O	ALA	182	26.316	16.815	72.654	1.00	29.66
ATOM	508	N	TYR	183	27.151	18.871	72.267	1.00	86.70
ATOM	509	CA	TYR	183	28.319	18.347	71.629	1.00	86.70
ATOM	510	CB	TYR	183	29.252	19.486	71.164	1.00	86.70
ATOM	511	CG	TYR	183	30.260	18.956	70.203	1.00	86.70
ATOM	512	CD1	TYR	183	29.917	18.769	68.883	1.00	86.70
ATOM	513	CD2	TYR	183	31.546	18.668	70.602	1.00	86.70
ATOM	514	CE1	TYR	183	30.830	18.288	67.975	1.00	86.70
ATOM	515	CE2	TYR	183	32.465	18.186	69.698	1.00	86.70
ATOM	516	CZ	TYR	183	32.109	17.994	68.385	1.00	86.70
ATOM	517	OH	TYR	183	33.050	17.500	67.457	1.00	86.70
ATOM	518	C	TYR	183	29.055	17.492	72.623	1.00	86.70
ATOM	519	O	TYR	183	29.454	16.371	72.316	1.00	86.70
ATOM	520	N	GLY	184	29.246	18.018	73.850	1.00	53.23
ATOM	521	CA	GLY	184	30.008	17.399	74.905	1.00	53.23
ATOM	522	C	GLY	184	29.405	16.176	75.549	1.00	53.23
ATOM	523	O	GLY	184	30.124	15.219	75.821	1.00	53.23

ATOM	524	N	SER	185	28.088	16.154	75.842	1.00120.41
ATOM	525	CA	SER	185	27.600	15.068	76.658	1.00120.41
ATOM	526	CB	SER	185	26.311	15.371	77.423	1.00120.41
ATOM	527	OG	SER	185	25.920	14.251	78.202	1.00120.41
ATOM	528	C	SER	185	27.382	13.816	75.878	1.00120.41
ATOM	529	O	SER	185	27.009	13.841	74.708	1.00120.41
ATOM	530	N	GLU	186	27.606	12.679	76.574	1.00233.92
ATOM	531	CA	GLU	186	27.606	11.349	76.034	1.00233.92
ATOM	532	CB	GLU	186	28.197	10.300	76.993	1.00233.92
ATOM	533	CG	GLU	186	27.438	10.153	78.313	1.00233.92
ATOM	534	CD	GLU	186	28.204	10.926	79.376	1.00233.92
ATOM	535	OE1	GLU	186	29.463	10.895	79.323	1.00233.92
ATOM	536	OE2	GLU	186	27.549	11.552	80.252	1.00233.92
ATOM	537	C	GLU	186	26.293	10.794	75.573	1.00233.92
ATOM	538	O	GLU	186	26.228	10.305	74.451	1.00233.92
ATOM	539	N	VAL	187	25.197	10.839	76.360	1.00129.80
ATOM	540	CA	VAL	187	24.082	10.104	75.822	1.00129.80
ATOM	541	CB	VAL	187	22.972	9.869	76.789	1.00129.80
ATOM	542	CG1	VAL	187	21.890	9.086	76.036	1.00129.80
ATOM	543	CG2	VAL	187	23.542	9.116	78.006	1.00129.80
ATOM	544	C	VAL	187	23.589	10.872	74.667	1.00129.80
ATOM	545	O	VAL	187	22.963	11.912	74.871	1.00129.80
ATOM	546	N	ASP	188	23.768	10.264	73.471	1.00 52.21
ATOM	547	CA	ASP	188	23.717	10.816	72.144	1.00 52.21
ATOM	548	CB	ASP	188	23.899	9.762	71.036	1.00 52.21
ATOM	549	CG	ASP	188	25.365	9.352	70.982	1.00 52.21
ATOM	550	OD1	ASP	188	26.195	10.032	71.642	1.00 52.21
ATOM	551	OD2	ASP	188	25.672	8.356	70.275	1.00 52.21
ATOM	552	C	ASP	188	22.449	11.526	71.851	1.00 52.21
ATOM	553	O	ASP	188	22.464	12.498	71.095	1.00 52.21
ATOM	554	N	TYR	189	21.319	11.067	72.403	1.00166.36
ATOM	555	CA	TYR	189	20.123	11.786	72.107	1.00166.36
ATOM	556	CB	TYR	189	18.831	11.184	72.665	1.00166.36
ATOM	557	CG	TYR	189	17.733	12.131	72.297	1.00166.36
ATOM	558	CD1	TYR	189	17.390	13.168	73.131	1.00166.36
ATOM	559	CD2	TYR	189	17.057	11.996	71.107	1.00166.36
ATOM	560	CE1	TYR	189	16.385	14.044	72.792	1.00166.36
ATOM	561	CE2	TYR	189	16.051	12.864	70.758	1.00166.36
ATOM	562	CZ	TYR	189	15.714	13.894	71.602	1.00166.36
ATOM	563	OH	TYR	189	14.682	14.789	71.248	1.00166.36
ATOM	564	C	TYR	189	20.307	13.168	72.624	1.00166.36
ATOM	565	O	TYR	189	19.731	14.076	72.027	1.00166.36
ATOM	566	N	ILE	190	21.118	13.292	73.723	1.00202.46
ATOM	567	CA	ILE	190	21.536	14.455	74.472	1.00202.46
ATOM	568	CB	ILE	190	23.029	14.604	74.460	1.00202.46
ATOM	569	CG2	ILE	190	23.560	14.232	73.064	1.00202.46
ATOM	570	CG1	ILE	190	23.425	15.999	74.936	1.00202.46
ATOM	571	CD1	ILE	190	24.932	16.231	74.971	1.00202.46
ATOM	572	C	ILE	190	21.016	15.628	73.777	1.00202.46
ATOM	573	O	ILE	190	21.551	16.067	72.761	1.00202.46
ATOM	574	N	GLY	191	19.934	16.184	74.316	1.00 65.34
ATOM	575	CA	GLY	191	19.400	17.209	73.507	1.00 65.34
ATOM	576	C	GLY	191	19.088	18.352	74.373	1.00 65.34
ATOM	577	O	GLY	191	18.357	18.240	75.355	1.00 65.34
ATOM	578	N	GLN	192	19.694	19.491	74.027	1.00 75.20
ATOM	579	CA	GLN	192	19.282	20.680	74.674	1.00 75.20
ATOM	580	CB	GLN	192	20.381	21.474	75.396	1.00 75.20
ATOM	581	CG	GLN	192	20.750	20.871	76.748	1.00 75.20
ATOM	582	CD	GLN	192	21.729	21.810	77.435	1.00 75.20
ATOM	583	OE1	GLN	192	22.084	22.849	76.882	1.00 75.20
ATOM	584	NE2	GLN	192	22.177	21.440	78.667	1.00 75.20
ATOM	585	C	GLN	192	18.705	21.484	73.573	1.00 75.20
ATOM	586	O	GLN	192	19.316	21.664	72.521	1.00 75.20
ATOM	587	N	PHE	193	17.460	21.929	73.771	1.00131.19
ATOM	588	CA	PHE	193	16.815	22.693	72.758	1.00131.19
ATOM	589	CB	PHE	193	15.278	22.596	72.752	1.00131.19

ATOM	590	CG	PHE	193	14.829	21.254	72.283	1.00131.19
ATOM	591	CD1	PHE	193	14.637	21.019	70.941	1.00131.19
ATOM	592	CD2	PHE	193	14.591	20.238	73.179	1.00131.19
ATOM	593	CE1	PHE	193	14.216	19.787	70.497	1.00131.19
ATOM	594	CE2	PHE	193	14.171	19.004	72.739	1.00131.19
ATOM	595	CZ	PHE	193	13.983	18.777	71.398	1.00131.19
ATOM	596	C	PHE	193	17.109	24.126	73.014	1.00131.19
ATOM	597	O	PHE	193	17.554	24.513	74.095	1.00131.19
ATOM	598	N	ASP	194	16.882	24.941	71.974	1.00136.05
ATOM	599	CA	ASP	194	16.986	26.361	72.067	1.00136.05
ATOM	600	CB	ASP	194	16.874	27.007	70.669	1.00136.05
ATOM	601	CG	ASP	194	16.238	26.078	69.643	1.00136.05
ATOM	602	OD1	ASP	194	15.729	24.995	70.027	1.00136.05
ATOM	603	OD2	ASP	194	16.250	26.455	68.441	1.00136.05
ATOM	604	C	ASP	194	15.780	26.756	72.873	1.00136.05
ATOM	605	O	ASP	194	14.927	25.924	73.178	1.00136.05
ATOM	606	N	MET	195	15.692	28.045	73.242	1.00 86.54
ATOM	607	CA	MET	195	14.641	28.631	74.023	1.00 86.54
ATOM	608	CB	MET	195	14.877	30.130	74.272	1.00 86.54
ATOM	609	CG	MET	195	13.675	30.836	74.900	1.00 86.54
ATOM	610	SD	MET	195	12.979	32.177	73.888	1.00 86.54
ATOM	611	CE	MET	195	11.417	32.271	74.814	1.00 86.54
ATOM	612	C	MET	195	13.348	28.535	73.274	1.00 86.54
ATOM	613	O	MET	195	12.282	28.438	73.881	1.00 86.54
ATOM	614	N	ARG	196	13.415	28.579	71.931	1.00106.06
ATOM	615	CA	ARG	196	12.260	28.602	71.075	1.00106.06
ATOM	616	CB	ARG	196	12.622	28.667	69.581	1.00106.06
ATOM	617	CG	ARG	196	13.170	30.024	69.130	1.00106.06
ATOM	618	CD	ARG	196	12.349	31.207	69.650	1.00106.06
ATOM	619	NE	ARG	196	11.021	31.185	68.972	1.00106.06
ATOM	620	CZ	ARG	196	10.079	32.124	69.285	1.00106.06
ATOM	621	NH1	ARG	196	10.355	33.094	70.209	1.00106.06
ATOM	622	NH2	ARG	196	8.857	32.094	68.677	1.00106.06
ATOM	623	C	ARG	196	11.425	27.371	71.275	1.00106.06
ATOM	624	O	ARG	196	10.203	27.423	71.145	1.00106.06
ATOM	625	N	PHE	197	12.058	26.231	71.600	1.00 81.65
ATOM	626	CA	PHE	197	11.374	24.977	71.747	1.00 81.65
ATOM	627	CB	PHE	197	12.338	23.902	72.276	1.00 81.65
ATOM	628	CG	PHE	197	11.562	22.710	72.718	1.00 81.65
ATOM	629	CD1	PHE	197	11.089	21.800	71.804	1.00 81.65
ATOM	630	CD2	PHE	197	11.325	22.497	74.059	1.00 81.65
ATOM	631	CE1	PHE	197	10.382	20.703	72.225	1.00 81.65
ATOM	632	CE2	PHE	197	10.617	21.397	74.486	1.00 81.65
ATOM	633	CZ	PHE	197	10.144	20.497	73.563	1.00 81.65
ATOM	634	C	PHE	197	10.260	25.112	72.737	1.00 81.65
ATOM	635	O	PHE	197	9.123	24.733	72.453	1.00 81.65
ATOM	636	N	LEU	198	10.546	25.674	73.923	1.00 91.14
ATOM	637	CA	LEU	198	9.522	25.774	74.919	1.00 91.14
ATOM	638	CB	LEU	198	9.988	26.424	76.224	1.00 91.14
ATOM	639	CG	LEU	198	8.832	26.534	77.232	1.00 91.14
ATOM	640	CD2	LEU	198	9.108	27.614	78.284	1.00 91.14
ATOM	641	CD1	LEU	198	8.452	25.160	77.810	1.00 91.14
ATOM	642	C	LEU	198	8.418	26.645	74.418	1.00 91.14
ATOM	643	O	LEU	198	7.243	26.337	74.610	1.00 91.14
ATOM	644	N	ASN	199	8.764	27.760	73.751	1.00 55.60
ATOM	645	CA	ASN	199	7.744	28.685	73.354	1.00 55.60
ATOM	646	CB	ASN	199	8.302	29.888	72.579	1.00 55.60
ATOM	647	CG	ASN	199	9.123	30.720	73.553	1.00 55.60
ATOM	648	OD1	ASN	199	10.349	30.767	73.468	1.00 55.60
ATOM	649	ND2	ASN	199	8.428	31.390	74.511	1.00 55.60
ATOM	650	C	ASN	199	6.765	27.995	72.457	1.00 55.60
ATOM	651	O	ASN	199	5.554	28.097	72.651	1.00 55.60
ATOM	652	N	SER	200	7.264	27.255	71.453	1.00 37.68
ATOM	653	CA	SER	200	6.381	26.626	70.516	1.00 37.68
ATOM	654	CB	SER	200	7.138	25.978	69.348	1.00 37.68
ATOM	655	OG	SER	200	7.729	26.981	68.534	1.00 37.68

ATOM	656	C	SER	200	5.567	25.572	71.203	1.00	37.68
ATOM	657	O	SER	200	4.366	25.448	70.962	1.00	37.68
ATOM	658	N	LEU	201	6.201	24.782	72.087	1.00	113.67
ATOM	659	CA	LEU	201	5.505	23.710	72.735	1.00	113.67
ATOM	660	CB	LEU	201	6.436	22.946	73.699	1.00	113.67
ATOM	661	CG	LEU	201	5.879	21.652	74.334	1.00	113.67
ATOM	662	CD2	LEU	201	5.647	20.569	73.270	1.00	113.67
ATOM	663	CD1	LEU	201	4.654	21.896	75.231	1.00	113.67
ATOM	664	C	LEU	201	4.402	24.300	73.551	1.00	113.67
ATOM	665	O	LEU	201	3.253	23.873	73.461	1.00	113.67
ATOM	666	N	ALA	202	4.738	25.309	74.375	1.00	48.96
ATOM	667	CA	ALA	202	3.776	25.881	75.269	1.00	48.96
ATOM	668	CB	ALA	202	4.412	26.873	76.260	1.00	48.96
ATOM	669	C	ALA	202	2.685	26.604	74.540	1.00	48.96
ATOM	670	O	ALA	202	1.507	26.362	74.793	1.00	48.96
ATOM	671	N	ILE	203	3.032	27.497	73.591	1.00	52.64
ATOM	672	CA	ILE	203	1.976	28.263	72.987	1.00	52.64
ATOM	673	CB	ILE	203	2.466	29.369	72.100	1.00	52.64
ATOM	674	CG2	ILE	203	1.239	29.999	71.423	1.00	52.64
ATOM	675	CG1	ILE	203	3.299	30.375	72.918	1.00	52.64
ATOM	676	CD1	ILE	203	4.098	31.354	72.060	1.00	52.64
ATOM	677	C	ILE	203	1.109	27.367	72.172	1.00	52.64
ATOM	678	O	ILE	203	-0.112	27.363	72.324	1.00	52.64
ATOM	679	N	HIS	204	1.721	26.555	71.293	1.00	151.99
ATOM	680	CA	HIS	204	0.914	25.674	70.508	1.00	151.99
ATOM	681	ND1	HIS	204	1.405	27.230	67.048	1.00	151.99
ATOM	682	CG	HIS	204	1.285	26.992	68.398	1.00	151.99
ATOM	683	CB	HIS	204	1.337	25.630	69.032	1.00	151.99
ATOM	684	NE2	HIS	204	1.157	29.214	68.026	1.00	151.99
ATOM	685	CD2	HIS	204	1.137	28.211	68.983	1.00	151.99
ATOM	686	CE1	HIS	204	1.320	28.578	66.883	1.00	151.99
ATOM	687	C	HIS	204	1.139	24.333	71.102	1.00	151.99
ATOM	688	O	HIS	204	1.898	23.522	70.574	1.00	151.99
ATOM	689	N	GLU	205	0.449	24.066	72.225	1.00	156.23
ATOM	690	CA	GLU	205	0.711	22.857	72.933	1.00	156.23
ATOM	691	CB	GLU	205	-0.210	22.672	74.150	1.00	156.23
ATOM	692	CG	GLU	205	0.028	21.351	74.885	1.00	156.23
ATOM	693	CD	GLU	205	-1.067	21.176	75.931	1.00	156.23
ATOM	694	OE1	GLU	205	-2.190	20.749	75.548	1.00	156.23
ATOM	695	OE2	GLU	205	-0.793	21.465	77.126	1.00	156.23
ATOM	696	C	GLU	205	0.462	21.702	72.042	1.00	156.23
ATOM	697	O	GLU	205	1.397	20.966	71.737	1.00	156.23
ATOM	698	N	LYS	206	-0.782	21.540	71.548	1.00	205.50
ATOM	699	CA	LYS	206	-1.007	20.396	70.719	1.00	205.50
ATOM	700	CB	LYS	206	-1.205	19.084	71.499	1.00	205.50
ATOM	701	CG	LYS	206	-0.059	18.679	72.424	1.00	205.50
ATOM	702	CD	LYS	206	-0.356	17.392	73.198	1.00	205.50
ATOM	703	CE	LYS	206	-1.759	17.342	73.812	1.00	205.50
ATOM	704	NZ	LYS	206	-1.795	18.114	75.073	1.00	205.50
ATOM	705	C	LYS	206	-2.308	20.561	70.016	1.00	205.50
ATOM	706	O	LYS	206	-3.343	20.732	70.658	1.00	205.50
ATOM	707	N	PHE	207	-2.301	20.529	68.671	1.00	72.61
ATOM	708	CA	PHE	207	-3.578	20.476	68.032	1.00	72.61
ATOM	709	CB	PHE	207	-3.496	20.581	66.501	1.00	72.61
ATOM	710	CG	PHE	207	-3.224	22.015	66.198	1.00	72.61
ATOM	711	CD1	PHE	207	-1.956	22.539	66.311	1.00	72.61
ATOM	712	CD2	PHE	207	-4.252	22.837	65.797	1.00	72.61
ATOM	713	CE1	PHE	207	-1.724	23.865	66.030	1.00	72.61
ATOM	714	CE2	PHE	207	-4.025	24.162	65.515	1.00	72.61
ATOM	715	CZ	PHE	207	-2.757	24.679	65.631	1.00	72.61
ATOM	716	C	PHE	207	-4.106	19.138	68.423	1.00	72.61
ATOM	717	O	PHE	207	-5.248	18.997	68.860	1.00	72.61
ATOM	718	N	ASP	208	-3.238	18.118	68.281	1.00	124.13
ATOM	719	CA	ASP	208	-3.514	16.787	68.731	1.00	124.13
ATOM	720	CB	ASP	208	-3.667	15.769	67.588	1.00	124.13
ATOM	721	CG	ASP	208	-5.011	16.013	66.921	1.00	124.13

ATOM	722	OD1	ASP	208	-5.724	16.956	67.359	1.00124.13
ATOM	723	OD2	ASP	208	-5.353	15.256	65.974	1.00124.13
ATOM	724	C	ASP	208	-2.297	16.402	69.506	1.00124.13
ATOM	725	O	ASP	208	-2.317	15.487	70.328	1.00124.13
ATOM	726	N	ALA	209	-1.197	17.135	69.250	1.00255.38
ATOM	727	CA	ALA	209	0.058	16.921	69.906	1.00255.38
ATOM	728	CB	ALA	209	0.844	15.720	69.354	1.00255.38
ATOM	729	C	ALA	209	0.860	18.146	69.624	1.00255.38
ATOM	730	O	ALA	209	0.424	18.995	68.849	1.00255.38
ATOM	731	N	PHE	210	2.040	18.286	70.266	1.00276.72
ATOM	732	CA	PHE	210	2.848	19.437	70.008	1.00276.72
ATOM	733	CB	PHE	210	3.978	19.598	71.040	1.00276.72
ATOM	734	CG	PHE	210	4.550	18.246	71.293	1.00276.72
ATOM	735	CD1	PHE	210	5.582	17.725	70.548	1.00276.72
ATOM	736	CD2	PHE	210	4.023	17.486	72.311	1.00276.72
ATOM	737	CE1	PHE	210	6.073	16.471	70.816	1.00276.72
ATOM	738	CE2	PHE	210	4.509	16.234	72.586	1.00276.72
ATOM	739	CZ	PHE	210	5.540	15.722	71.837	1.00276.72
ATOM	740	C	PHE	210	3.365	19.370	68.611	1.00276.72
ATOM	741	O	PHE	210	4.441	18.848	68.335	1.00276.72
ATOM	742	N	MET	211	2.563	19.920	67.681	1.00 90.31
ATOM	743	CA	MET	211	2.873	19.955	66.287	1.00 90.31
ATOM	744	CB	MET	211	1.723	20.500	65.422	1.00 90.31
ATOM	745	CG	MET	211	0.500	19.583	65.367	1.00 90.31
ATOM	746	SD	MET	211	-0.869	20.212	64.350	1.00 90.31
ATOM	747	CE	MET	211	0.015	20.005	62.774	1.00 90.31
ATOM	748	C	MET	211	4.031	20.863	66.088	1.00 90.31
ATOM	749	O	MET	211	4.908	20.603	65.265	1.00 90.31
ATOM	750	N	ASN	212	4.062	21.973	66.845	1.00 90.13
ATOM	751	CA	ASN	212	5.123	22.906	66.637	1.00 90.13
ATOM	752	CB	ASN	212	4.978	24.204	67.447	1.00 90.13
ATOM	753	CG	ASN	212	5.890	25.234	66.791	1.00 90.13
ATOM	754	OD1	ASN	212	7.077	24.987	66.582	1.00 90.13
ATOM	755	ND2	ASN	212	5.326	26.423	66.457	1.00 90.13
ATOM	756	C	ASN	212	6.400	22.233	67.018	1.00 90.13
ATOM	757	O	ASN	212	7.441	22.475	66.413	1.00 90.13
ATOM	758	N	LYS	213	6.345	21.424	68.092	1.00142.77
ATOM	759	CA	LYS	213	7.426	20.654	68.651	1.00142.77
ATOM	760	CB	LYS	213	7.131	20.197	70.088	1.00142.77
ATOM	761	CG	LYS	213	8.178	19.226	70.645	1.00142.77
ATOM	762	CD	LYS	213	8.019	18.934	72.136	1.00142.77
ATOM	763	CE	LYS	213	8.827	17.726	72.617	1.00142.77
ATOM	764	NZ	LYS	213	10.230	17.810	72.158	1.00142.77
ATOM	765	C	LYS	213	7.773	19.407	67.888	1.00142.77
ATOM	766	O	LYS	213	8.928	18.987	67.896	1.00142.77
ATOM	767	N	HIS	214	6.801	18.776	67.202	1.00151.89
ATOM	768	CA	HIS	214	6.993	17.422	66.740	1.00151.89
ATOM	769	ND1	HIS	214	6.475	16.168	63.639	1.00151.89
ATOM	770	CG	HIS	214	5.807	17.013	64.500	1.00151.89
ATOM	771	CB	HIS	214	5.781	16.828	65.991	1.00151.89
ATOM	772	NE2	HIS	214	5.499	17.715	62.378	1.00151.89
ATOM	773	CD2	HIS	214	5.217	17.953	63.712	1.00151.89
ATOM	774	CE1	HIS	214	6.256	16.634	62.383	1.00151.89
ATOM	775	C	HIS	214	8.196	17.269	65.858	1.00151.89
ATOM	776	O	HIS	214	8.878	16.248	65.927	1.00151.89
ATOM	777	N	ILE	215	8.480	18.263	65.001	1.00101.59
ATOM	778	CA	ILE	215	9.542	18.215	64.031	1.00101.59
ATOM	779	CB	ILE	215	9.561	19.420	63.133	1.00101.59
ATOM	780	CG2	ILE	215	9.891	20.656	63.989	1.00101.59
ATOM	781	CG1	ILE	215	10.536	19.201	61.965	1.00101.59
ATOM	782	CD1	ILE	215	10.425	20.268	60.876	1.00101.59
ATOM	783	C	ILE	215	10.905	18.140	64.654	1.00101.59
ATOM	784	O	ILE	215	11.780	17.444	64.142	1.00101.59
ATOM	785	N	LEU	216	11.122	18.846	65.777	1.00 71.07
ATOM	786	CA	LEU	216	12.441	19.086	66.298	1.00 71.07
ATOM	787	CB	LEU	216	12.443	19.971	67.554	1.00 71.07

ATOM	788	CG	LEU	216	11.974	21.411	67.274	1.00	71.07
ATOM	789	CD2	LEU	216	12.717	22.018	66.072	1.00	71.07
ATOM	790	CD1	LEU	216	12.062	22.281	68.538	1.00	71.07
ATOM	791	C	LEU	216	13.245	17.858	66.614	1.00	71.07
ATOM	792	O	LEU	216	14.434	17.832	66.307	1.00	71.07
ATOM	793	N	SER	217	12.668	16.807	67.217	1.00	91.67
ATOM	794	CA	SER	217	13.489	15.691	67.605	1.00	91.67
ATOM	795	CB	SER	217	12.686	14.580	68.299	1.00	91.67
ATOM	796	OG	SER	217	11.706	14.060	67.415	1.00	91.67
ATOM	797	C	SER	217	14.146	15.102	66.396	1.00	91.67
ATOM	798	O	SER	217	15.287	14.648	66.461	1.00	91.67
ATOM	799	N	TYR	218	13.450	15.117	65.249	1.00	91.93
ATOM	800	CA	TYR	218	13.967	14.526	64.052	1.00	91.93
ATOM	801	CB	TYR	218	12.965	14.580	62.887	1.00	91.93
ATOM	802	CG	TYR	218	13.598	13.904	61.723	1.00	91.93
ATOM	803	CD1	TYR	218	13.594	12.531	61.639	1.00	91.93
ATOM	804	CD2	TYR	218	14.187	14.636	60.716	1.00	91.93
ATOM	805	CE1	TYR	218	14.172	11.891	60.569	1.00	91.93
ATOM	806	CE2	TYR	218	14.768	14.000	59.643	1.00	91.93
ATOM	807	CZ	TYR	218	14.759	12.628	59.569	1.00	91.93
ATOM	808	OH	TYR	218	15.351	11.972	58.470	1.00	91.93
ATOM	809	C	TYR	218	15.220	15.241	63.624	1.00	91.93
ATOM	810	O	TYR	218	16.187	14.600	63.215	1.00	91.93
ATOM	811	N	ILE	219	15.247	16.586	63.726	1.00	130.52
ATOM	812	CA	ILE	219	16.367	17.377	63.277	1.00	130.52
ATOM	813	CB	ILE	219	16.191	18.863	63.444	1.00	130.52
ATOM	814	CG2	ILE	219	16.362	19.210	64.932	1.00	130.52
ATOM	815	CG1	ILE	219	17.184	19.615	62.541	1.00	130.52
ATOM	816	CD1	ILE	219	16.896	19.452	61.050	1.00	130.52
ATOM	817	C	ILE	219	17.573	16.969	64.061	1.00	130.52
ATOM	818	O	ILE	219	18.698	17.008	63.569	1.00	130.52
ATOM	819	N	LEU	220	17.348	16.588	65.328	1.00	154.16
ATOM	820	CA	LEU	220	18.369	16.162	66.239	1.00	154.16
ATOM	821	CB	LEU	220	17.799	15.834	67.629	1.00	154.16
ATOM	822	CG	LEU	220	18.840	15.357	68.658	1.00	154.16
ATOM	823	CD2	LEU	220	18.145	14.815	69.913	1.00	154.16
ATOM	824	CD1	LEU	220	19.877	16.451	68.974	1.00	154.16
ATOM	825	C	LEU	220	18.998	14.921	65.676	1.00	154.16
ATOM	826	O	LEU	220	20.148	14.608	65.984	1.00	154.16
ATOM	827	N	LYS	221	18.239	14.166	64.850	1.00	116.78
ATOM	828	CA	LYS	221	18.713	12.951	64.248	1.00	116.78
ATOM	829	CB	LYS	221	20.010	13.104	63.431	1.00	116.78
ATOM	830	CG	LYS	221	19.781	13.446	61.955	1.00	116.78
ATOM	831	CD	LYS	221	19.173	14.823	61.684	1.00	116.78
ATOM	832	CE	LYS	221	18.960	15.100	60.193	1.00	116.78
ATOM	833	NZ	LYS	221	18.364	16.442	60.003	1.00	116.78
ATOM	834	C	LYS	221	18.933	11.916	65.294	1.00	116.78
ATOM	835	O	LYS	221	19.776	11.032	65.143	1.00	116.78
ATOM	836	N	ASP	222	18.163	11.994	66.391	1.00	95.70
ATOM	837	CA	ASP	222	18.285	10.985	67.390	1.00	95.70
ATOM	838	CB	ASP	222	19.088	11.446	68.619	1.00	95.70
ATOM	839	CG	ASP	222	19.764	10.227	69.239	1.00	95.70
ATOM	840	OD1	ASP	222	19.230	9.095	69.101	1.00	95.70
ATOM	841	OD2	ASP	222	20.850	10.418	69.847	1.00	95.70
ATOM	842	C	ASP	222	16.884	10.667	67.806	1.00	95.70
ATOM	843	O	ASP	222	15.936	11.314	67.355	1.00	95.70
ATOM	844	N	LYS	223	16.713	9.632	68.651	1.00	73.05
ATOM	845	CA	LYS	223	15.410	9.247	69.104	1.00	73.05
ATOM	846	CB	LYS	223	15.081	7.777	68.786	1.00	73.05
ATOM	847	CG	LYS	223	14.980	7.499	67.283	1.00	73.05
ATOM	848	CD	LYS	223	14.994	6.012	66.915	1.00	73.05
ATOM	849	CE	LYS	223	16.395	5.438	66.695	1.00	73.05
ATOM	850	NZ	LYS	223	16.301	4.004	66.340	1.00	73.05
ATOM	851	C	LYS	223	15.387	9.406	70.594	1.00	73.05
ATOM	852	O	LYS	223	16.419	9.335	71.254	1.00	73.05
ATOM	853	N	ILE	224	14.179	9.594	71.156	1.00	70.41

ATOM	854	CA	ILE	224	13.955	9.832	72.556	1.00	70.41
ATOM	855	CB	ILE	224	12.504	10.030	72.899	1.00	70.41
ATOM	856	CG2	ILE	224	11.747	8.727	72.591	1.00	70.41
ATOM	857	CG1	ILE	224	12.359	10.508	74.355	1.00	70.41
ATOM	858	CD1	ILE	224	10.944	10.955	74.720	1.00	70.41
ATOM	859	C	ILE	224	14.450	8.672	73.367	1.00	70.41
ATOM	860	O	ILE	224	14.951	8.850	74.474	1.00	70.41
ATOM	861	N	LYS	225	14.307	7.443	72.851	1.00	97.06
ATOM	862	CA	LYS	225	14.661	6.273	73.604	1.00	97.06
ATOM	863	CB	LYS	225	14.480	4.980	72.798	1.00	97.06
ATOM	864	CG	LYS	225	13.054	4.737	72.315	1.00	97.06
ATOM	865	CD	LYS	225	12.965	3.668	71.226	1.00	97.06
ATOM	866	CE	LYS	225	12.377	2.339	71.707	1.00	97.06
ATOM	867	NZ	LYS	225	13.256	1.731	72.729	1.00	97.06
ATOM	868	C	LYS	225	16.112	6.313	73.984	1.00	97.06
ATOM	869	O	LYS	225	16.470	5.922	75.093	1.00	97.06
ATOM	870	N	SER	226	16.990	6.764	73.069	1.00	90.97
ATOM	871	CA	SER	226	18.410	6.730	73.291	1.00	90.97
ATOM	872	CB	SER	226	19.215	6.979	72.004	1.00	90.97
ATOM	873	OG	SER	226	20.605	6.933	72.287	1.00	90.97
ATOM	874	C	SER	226	18.870	7.741	74.308	1.00	90.97
ATOM	875	O	SER	226	19.916	7.548	74.922	1.00	90.97
ATOM	876	N	SER	227	18.108	8.833	74.522	1.00	110.32
ATOM	877	CA	SER	227	18.499	9.964	75.332	1.00	110.32
ATOM	878	CB	SER	227	17.489	11.119	75.265	1.00	110.32
ATOM	879	OG	SER	227	17.924	12.201	76.073	1.00	110.32
ATOM	880	C	SER	227	18.633	9.705	76.797	1.00	110.32
ATOM	881	O	SER	227	17.830	9.000	77.407	1.00	110.32
ATOM	882	N	THR	228	19.720	10.255	77.385	1.00	135.76
ATOM	883	CA	THR	228	19.856	10.302	78.811	1.00	135.76
ATOM	884	CB	THR	228	21.272	10.507	79.277	1.00	135.76
ATOM	885	OG1	THR	228	21.325	10.466	80.694	1.00	135.76
ATOM	886	CG2	THR	228	21.813	11.846	78.754	1.00	135.76
ATOM	887	C	THR	228	19.027	11.446	79.317	1.00	135.76
ATOM	888	O	THR	228	18.300	11.315	80.302	1.00	135.76
ATOM	889	N	SER	229	19.099	12.611	78.627	1.00	65.15
ATOM	890	CA	SER	229	18.361	13.736	79.125	1.00	65.15
ATOM	891	CB	SER	229	19.084	14.485	80.257	1.00	65.15
ATOM	892	OG	SER	229	19.237	13.627	81.380	1.00	65.15
ATOM	893	C	SER	229	18.107	14.715	78.024	1.00	65.15
ATOM	894	O	SER	229	18.783	14.717	76.997	1.00	65.15
ATOM	895	N	ARG	230	17.077	15.563	78.221	1.00	127.75
ATOM	896	CA	ARG	230	16.743	16.612	77.300	1.00	127.75
ATOM	897	CB	ARG	230	15.367	16.447	76.627	1.00	127.75
ATOM	898	CG	ARG	230	15.036	17.576	75.646	1.00	127.75
ATOM	899	CD	ARG	230	13.546	17.698	75.313	1.00	127.75
ATOM	900	NE	ARG	230	12.897	18.416	76.447	1.00	127.75
ATOM	901	CZ	ARG	230	12.371	17.715	77.493	1.00	127.75
ATOM	902	NH1	ARG	230	12.392	16.351	77.471	1.00	127.75
ATOM	903	NH2	ARG	230	11.832	18.376	78.560	1.00	127.75
ATOM	904	C	ARG	230	16.645	17.861	78.123	1.00	127.75
ATOM	905	O	ARG	230	15.977	17.874	79.157	1.00	127.75
ATOM	906	N	PHE	231	17.305	18.954	77.685	1.00	65.40
ATOM	907	CA	PHE	231	17.235	20.164	78.456	1.00	65.40
ATOM	908	CB	PHE	231	18.604	20.799	78.762	1.00	65.40
ATOM	909	CG	PHE	231	19.378	19.907	79.674	1.00	65.40
ATOM	910	CD1	PHE	231	20.144	18.876	79.175	1.00	65.40
ATOM	911	CD2	PHE	231	19.351	20.109	81.034	1.00	65.40
ATOM	912	CE1	PHE	231	20.861	18.059	80.020	1.00	65.40
ATOM	913	CE2	PHE	231	20.064	19.295	81.882	1.00	65.40
ATOM	914	CZ	PHE	231	20.824	18.268	81.377	1.00	65.40
ATOM	915	C	PHE	231	16.455	21.183	77.681	1.00	65.40
ATOM	916	O	PHE	231	16.590	21.284	76.464	1.00	65.40
ATOM	917	N	VAL	232	15.583	21.955	78.365	1.00	54.92
ATOM	918	CA	VAL	232	14.876	22.976	77.648	1.00	54.92
ATOM	919	CB	VAL	232	13.409	22.698	77.490	1.00	54.92

ATOM	920	CG1	VAL	232	12.754	23.898	76.786	1.00	54.92
ATOM	921	CG2	VAL	232	13.244	21.370	76.736	1.00	54.92
ATOM	922	C	VAL	232	15.011	24.260	78.404	1.00	54.92
ATOM	923	O	VAL	232	14.491	24.399	79.511	1.00	54.92
ATOM	924	N	MET	233	15.697	25.250	77.798	1.00161.31	
ATOM	925	CA	MET	233	15.841	26.540	78.406	1.00161.31	
ATOM	926	CB	MET	233	16.866	27.450	77.708	1.00161.31	
ATOM	927	CG	MET	233	18.319	27.051	77.977	1.00161.31	
ATOM	928	SD	MET	233	18.818	25.457	77.264	1.00161.31	
ATOM	929	CE	MET	233	18.262	24.451	78.667	1.00161.31	
ATOM	930	C	MET	233	14.501	27.185	78.306	1.00161.31	
ATOM	931	O	MET	233	13.759	26.978	77.345	1.00161.31	
ATOM	932	N	PHE	234	14.169	27.997	79.320	1.00157.04	
ATOM	933	CA	PHE	234	12.858	28.548	79.456	1.00157.04	
ATOM	934	CB	PHE	234	12.307	28.180	80.844	1.00157.04	
ATOM	935	CG	PHE	234	10.873	28.528	80.992	1.00157.04	
ATOM	936	CD1	PHE	234	10.467	29.841	81.006	1.00157.04	
ATOM	937	CD2	PHE	234	9.932	27.532	81.104	1.00157.04	
ATOM	938	CE1	PHE	234	9.138	30.162	81.142	1.00157.04	
ATOM	939	CE2	PHE	234	8.605	27.851	81.243	1.00157.04	
ATOM	940	CZ	PHE	234	8.202	29.165	81.262	1.00157.04	
ATOM	941	C	PHE	234	12.977	30.035	79.439	1.00157.04	
ATOM	942	O	PHE	234	13.862	30.610	80.072	1.00157.04	
ATOM	943	N	GLY	235	12.069	30.702	78.707	1.00	36.60
ATOM	944	CA	GLY	235	12.071	32.130	78.725	1.00	36.60
ATOM	945	C	GLY	235	10.788	32.496	79.392	1.00	36.60
ATOM	946	O	GLY	235	9.740	31.923	79.098	1.00	36.60
ATOM	947	N	PHE	236	10.847	33.476	80.310	1.00124.45	
ATOM	948	CA	PHE	236	9.688	33.908	81.033	1.00124.45	
ATOM	949	CB	PHE	236	10.025	34.424	82.451	1.00124.45	
ATOM	950	CG	PHE	236	8.777	34.878	83.134	1.00124.45	
ATOM	951	CD1	PHE	236	7.844	33.978	83.598	1.00124.45	
ATOM	952	CD2	PHE	236	8.552	36.220	83.328	1.00124.45	
ATOM	953	CE1	PHE	236	6.701	34.418	84.226	1.00124.45	
ATOM	954	CE2	PHE	236	7.412	36.666	83.956	1.00124.45	
ATOM	955	CZ	PHE	236	6.480	35.762	84.406	1.00124.45	
ATOM	956	C	PHE	236	9.074	35.005	80.228	1.00124.45	
ATOM	957	O	PHE	236	9.718	35.532	79.322	1.00124.45	
ATOM	958	N	CYS	237	7.805	35.361	80.530	1.00168.32	
ATOM	959	CA	CYS	237	7.128	36.378	79.777	1.00168.32	
ATOM	960	CB	CYS	237	5.751	36.753	80.352	1.00168.32	
ATOM	961	SG	CYS	237	4.549	35.394	80.243	1.00168.32	
ATOM	962	C	CYS	237	7.986	37.583	79.865	1.00168.32	
ATOM	963	O	CYS	237	8.268	38.226	78.854	1.00168.32	
ATOM	964	N	TYR	238	8.442	37.926	81.081	1.00284.30	
ATOM	965	CA	TYR	238	9.416	38.961	81.072	1.00284.30	
ATOM	966	CB	TYR	238	9.903	39.425	82.462	1.00284.30	
ATOM	967	CG	TYR	238	8.854	40.286	83.078	1.00284.30	
ATOM	968	CD1	TYR	238	8.763	41.610	82.716	1.00284.30	
ATOM	969	CD2	TYR	238	7.978	39.791	84.017	1.00284.30	
ATOM	970	CE1	TYR	238	7.806	42.429	83.266	1.00284.30	
ATOM	971	CE2	TYR	238	7.018	40.607	84.574	1.00284.30	
ATOM	972	CZ	TYR	238	6.932	41.927	84.199	1.00284.30	
ATOM	973	OH	TYR	238	5.948	42.765	84.766	1.00284.30	
ATOM	974	C	TYR	238	10.554	38.314	80.372	1.00284.30	
ATOM	975	O	TYR	238	10.991	37.226	80.741	1.00284.30	
ATOM	976	N	LEU	239	11.055	38.973	79.320	1.00171.87	
ATOM	977	CA	LEU	239	12.103	38.407	78.536	1.00171.87	
ATOM	978	CB	LEU	239	12.501	39.289	77.341	1.00171.87	
ATOM	979	CG	LEU	239	12.683	40.775	77.715	1.00171.87	
ATOM	980	CD2	LEU	239	11.503	41.296	78.551	1.00171.87	
ATOM	981	CD1	LEU	239	12.953	41.633	76.469	1.00171.87	
ATOM	982	C	LEU	239	13.273	38.263	79.446	1.00171.87	
ATOM	983	O	LEU	239	14.132	37.407	79.253	1.00171.87	
ATOM	984	N	SER	240	13.308	39.118	80.478	1.00119.68	
ATOM	985	CA	SER	240	14.403	39.216	81.390	1.00119.68	

ATOM	986	CB	SER	240	14.206	40.338	82.423	1.00119.68
ATOM	987	OG	SER	240	15.316	40.390	83.307	1.00119.68
ATOM	988	C	SER	240	14.663	37.940	82.151	1.00119.68
ATOM	989	O	SER	240	15.794	37.735	82.584	1.00119.68
ATOM	990	N	HIS	241	13.682	37.034	82.352	1.00100.43
ATOM	991	CA	HIS	241	14.003	35.901	83.190	1.00100.43
ATOM	992	ND1	HIS	241	13.297	33.116	84.774	1.00100.43
ATOM	993	CG	HIS	241	13.303	34.445	85.135	1.00100.43
ATOM	994	CB	HIS	241	12.906	35.559	84.213	1.00100.43
ATOM	995	NE2	HIS	241	14.003	33.198	86.881	1.00100.43
ATOM	996	CD2	HIS	241	13.736	34.477	86.425	1.00100.43
ATOM	997	CE1	HIS	241	13.724	32.415	85.855	1.00100.43
ATOM	998	C	HIS	241	14.250	34.656	82.382	1.00100.43
ATOM	999	O	HIS	241	13.594	34.412	81.371	1.00100.43
ATOM	1000	N	TRP	242	15.237	33.839	82.828	1.00 71.70
ATOM	1001	CA	TRP	242	15.568	32.596	82.183	1.00 71.70
ATOM	1002	CB	TRP	242	16.978	32.577	81.559	1.00 71.70
ATOM	1003	CG	TRP	242	17.211	31.501	80.518	1.00 71.70
ATOM	1004	CD2	TRP	242	16.960	30.110	80.750	1.00 71.70
ATOM	1005	CD1	TRP	242	17.689	31.602	79.246	1.00 71.70
ATOM	1006	NE1	TRP	242	17.753	30.353	78.668	1.00 71.70
ATOM	1007	CE2	TRP	242	17.306	29.425	79.588	1.00 71.70
ATOM	1008	CE3	TRP	242	16.483	29.452	81.849	1.00 71.70
ATOM	1009	CZ2	TRP	242	17.180	28.067	79.501	1.00 71.70
ATOM	1010	CZ3	TRP	242	16.352	28.085	81.760	1.00 71.70
ATOM	1011	CH2	TRP	242	16.694	27.406	80.610	1.00 71.70
ATOM	1012	C	TRP	242	15.543	31.511	83.223	1.00 71.70
ATOM	1013	O	TRP	242	16.038	31.691	84.334	1.00 71.70
ATOM	1014	N	LYS	243	14.954	30.348	82.873	1.00134.01
ATOM	1015	CA	LYS	243	14.840	29.232	83.772	1.00134.01
ATOM	1016	CB	LYS	243	13.473	29.195	84.481	1.00134.01
ATOM	1017	CG	LYS	243	12.291	29.385	83.532	1.00134.01
ATOM	1018	CD	LYS	243	10.931	29.354	84.229	1.00134.01
ATOM	1019	CE	LYS	243	10.595	30.669	84.937	1.00134.01
ATOM	1020	NZ	LYS	243	9.215	30.623	85.468	1.00134.01
ATOM	1021	C	LYS	243	15.057	27.987	82.960	1.00134.01
ATOM	1022	O	LYS	243	15.282	28.077	81.755	1.00134.01
ATOM	1023	N	CYS	244	15.048	26.787	83.586	1.00 62.56
ATOM	1024	CA	CYS	244	15.340	25.638	82.771	1.00 62.56
ATOM	1025	CB	CYS	244	16.815	25.213	82.855	1.00 62.56
ATOM	1026	SG	CYS	244	17.198	23.765	81.826	1.00 62.56
ATOM	1027	C	CYS	244	14.518	24.452	83.180	1.00 62.56
ATOM	1028	O	CYS	244	14.132	24.296	84.337	1.00 62.56
ATOM	1029	N	VAL	245	14.220	23.573	82.204	1.00105.02
ATOM	1030	CA	VAL	245	13.522	22.360	82.509	1.00105.02
ATOM	1031	CB	VAL	245	12.237	22.162	81.758	1.00105.02
ATOM	1032	CG1	VAL	245	11.241	23.250	82.186	1.00105.02
ATOM	1033	CG2	VAL	245	12.541	22.149	80.254	1.00105.02
ATOM	1034	C	VAL	245	14.437	21.242	82.137	1.00105.02
ATOM	1035	O	VAL	245	15.161	21.330	81.145	1.00105.02
ATOM	1036	N	ILE	246	14.469	20.170	82.956	1.00 69.99
ATOM	1037	CA	ILE	246	15.311	19.068	82.601	1.00 69.99
ATOM	1038	CB	ILE	246	16.362	18.704	83.605	1.00 69.99
ATOM	1039	CG2	ILE	246	17.040	17.415	83.114	1.00 69.99
ATOM	1040	CG1	ILE	246	17.357	19.840	83.845	1.00 69.99
ATOM	1041	CD1	ILE	246	18.356	19.453	84.928	1.00 69.99
ATOM	1042	C	ILE	246	14.466	17.845	82.536	1.00 69.99
ATOM	1043	O	ILE	246	13.752	17.519	83.483	1.00 69.99
ATOM	1044	N	TYR	247	14.526	17.118	81.409	1.00162.63
ATOM	1045	CA	TYR	247	13.821	15.877	81.419	1.00162.63
ATOM	1046	CB	TYR	247	12.993	15.571	80.164	1.00162.63
ATOM	1047	CG	TYR	247	12.404	14.225	80.410	1.00162.63
ATOM	1048	CD1	TYR	247	11.304	14.083	81.227	1.00162.63
ATOM	1049	CD2	TYR	247	12.952	13.106	79.831	1.00162.63
ATOM	1050	CE1	TYR	247	10.760	12.842	81.461	1.00162.63
ATOM	1051	CE2	TYR	247	12.411	11.864	80.062	1.00162.63

ATOM	1052	CZ	TYR	247	11.313	11.730	80.876	1.00162.63
ATOM	1053	OH	TYR	247	10.760	10.453	81.111	1.00162.63
ATOM	1054	C	TYR	247	14.873	14.832	81.502	1.00162.63
ATOM	1055	O	TYR	247	15.725	14.720	80.623	1.00162.63
ATOM	1056	N	ASP	248	14.861	14.054	82.598	1.00120.84
ATOM	1057	CA	ASP	248	15.853	13.040	82.731	1.00120.84
ATOM	1058	CB	ASP	248	16.545	13.029	84.105	1.00120.84
ATOM	1059	CG	ASP	248	15.489	12.886	85.182	1.00120.84
ATOM	1060	OD1	ASP	248	15.119	11.728	85.497	1.00120.84
ATOM	1061	OD2	ASP	248	15.045	13.937	85.714	1.00120.84
ATOM	1062	C	ASP	248	15.220	11.721	82.447	1.00120.84
ATOM	1063	O	ASP	248	14.346	11.239	83.161	1.00120.84
ATOM	1064	N	LYS	249	15.627	11.115	81.325	1.00137.23
ATOM	1065	CA	LYS	249	15.099	9.839	80.954	1.00137.23
ATOM	1066	CB	LYS	249	15.586	9.390	79.563	1.00137.23
ATOM	1067	CG	LYS	249	15.422	7.890	79.295	1.00137.23
ATOM	1068	CD	LYS	249	13.983	7.378	79.300	1.00137.23
ATOM	1069	CE	LYS	249	13.903	5.865	79.081	1.00137.23
ATOM	1070	NZ	LYS	249	12.538	5.377	79.380	1.00137.23
ATOM	1071	C	LYS	249	15.536	8.806	81.941	1.00137.23
ATOM	1072	O	LYS	249	14.751	7.941	82.325	1.00137.23
ATOM	1073	N	LYS	250	16.810	8.864	82.375	1.00140.70
ATOM	1074	CA	LYS	250	17.312	7.828	83.232	1.00140.70
ATOM	1075	CB	LYS	250	18.817	7.965	83.526	1.00140.70
ATOM	1076	CG	LYS	250	19.206	9.188	84.359	1.00140.70
ATOM	1077	CD	LYS	250	20.614	9.087	84.948	1.00140.70
ATOM	1078	CE	LYS	250	21.722	9.373	83.934	1.00140.70
ATOM	1079	NZ	LYS	250	21.855	10.833	83.730	1.00140.70
ATOM	1080	C	LYS	250	16.603	7.804	84.555	1.00140.70
ATOM	1081	O	LYS	250	16.115	6.759	84.982	1.00140.70
ATOM	1082	N	GLN	251	16.534	8.962	85.239	1.00123.46
ATOM	1083	CA	GLN	251	15.928	9.069	86.537	1.00123.46
ATOM	1084	CB	GLN	251	16.416	10.269	87.378	1.00123.46
ATOM	1085	CG	GLN	251	15.776	10.383	88.762	1.00123.46
ATOM	1086	CD	GLN	251	16.494	11.496	89.518	1.00123.46
ATOM	1087	OE1	GLN	251	15.986	12.034	90.499	1.00123.46
ATOM	1088	NE2	GLN	251	17.723	11.844	89.053	1.00123.46
ATOM	1089	C	GLN	251	14.433	9.026	86.417	1.00123.46
ATOM	1090	O	GLN	251	13.737	8.731	87.387	1.00123.46
ATOM	1091	N	CYS	252	13.900	9.307	85.212	1.00 57.14
ATOM	1092	CA	CYS	252	12.481	9.332	85.003	1.00 57.14
ATOM	1093	CB	CYS	252	11.792	8.009	85.384	1.00 57.14
ATOM	1094	SG	CYS	252	12.283	6.624	84.314	1.00 57.14
ATOM	1095	C	CYS	252	11.864	10.429	85.808	1.00 57.14
ATOM	1096	O	CYS	252	10.816	10.259	86.429	1.00 57.14
ATOM	1097	N	LEU	253	12.527	11.600	85.826	1.00 58.16
ATOM	1098	CA	LEU	253	11.977	12.742	86.490	1.00 58.16
ATOM	1099	CB	LEU	253	12.742	13.160	87.761	1.00 58.16
ATOM	1100	CG	LEU	253	12.666	12.118	88.897	1.00 58.16
ATOM	1101	CD2	LEU	253	11.225	11.641	89.125	1.00 58.16
ATOM	1102	CD1	LEU	253	13.328	12.646	90.181	1.00 58.16
ATOM	1103	C	LEU	253	11.998	13.897	85.533	1.00 58.16
ATOM	1104	O	LEU	253	12.768	13.915	84.572	1.00 58.16
ATOM	1105	N	VAL	254	11.093	14.870	85.756	1.00 54.62
ATOM	1106	CA	VAL	254	11.055	16.079	84.986	1.00 54.62
ATOM	1107	CB	VAL	254	9.737	16.349	84.318	1.00 54.62
ATOM	1108	CG1	VAL	254	9.768	17.773	83.745	1.00 54.62
ATOM	1109	CG2	VAL	254	9.498	15.270	83.249	1.00 54.62
ATOM	1110	C	VAL	254	11.251	17.154	85.994	1.00 54.62
ATOM	1111	O	VAL	254	10.523	17.214	86.985	1.00 54.62
ATOM	1112	N	SER	255	12.232	18.045	85.775	1.00 89.13
ATOM	1113	CA	SER	255	12.477	18.995	86.812	1.00 89.13
ATOM	1114	CB	SER	255	13.855	18.822	87.471	1.00 89.13
ATOM	1115	OG	SER	255	13.919	17.580	88.156	1.00 89.13
ATOM	1116	C	SER	255	12.418	20.377	86.264	1.00 89.13
ATOM	1117	O	SER	255	12.668	20.611	85.081	1.00 89.13

ATOM	1118	N	PHE	256	12.042	21.321	87.151	1.00	81.52
ATOM	1119	CA	PHE	256	11.974	22.719	86.856	1.00	81.52
ATOM	1120	CB	PHE	256	10.587	23.303	87.192	1.00	81.52
ATOM	1121	CG	PHE	256	10.553	24.775	86.949	1.00	81.52
ATOM	1122	CD1	PHE	256	10.544	25.283	85.670	1.00	81.52
ATOM	1123	CD2	PHE	256	10.493	25.650	88.011	1.00	81.52
ATOM	1124	CE1	PHE	256	10.502	26.641	85.457	1.00	81.52
ATOM	1125	CE2	PHE	256	10.450	27.009	87.805	1.00	81.52
ATOM	1126	CZ	PHE	256	10.457	27.507	86.524	1.00	81.52
ATOM	1127	C	PHE	256	12.995	23.343	87.754	1.00	81.52
ATOM	1128	O	PHE	256	12.908	23.224	88.974	1.00	81.52
ATOM	1129	N	TYR	257	13.991	24.020	87.148	1.00	150.24
ATOM	1130	CA	TYR	257	15.109	24.629	87.809	1.00	150.24
ATOM	1131	CB	TYR	257	16.428	24.122	87.204	1.00	150.24
ATOM	1132	CG	TYR	257	17.512	25.123	87.394	1.00	150.24
ATOM	1133	CD1	TYR	257	18.208	25.218	88.567	1.00	150.24
ATOM	1134	CD2	TYR	257	17.837	25.972	86.361	1.00	150.24
ATOM	1135	CE1	TYR	257	19.206	26.151	88.715	1.00	150.24
ATOM	1136	CE2	TYR	257	18.832	26.908	86.498	1.00	150.24
ATOM	1137	CZ	TYR	257	19.522	26.996	87.681	1.00	150.24
ATOM	1138	OH	TYR	257	20.546	27.950	87.840	1.00	150.24
ATOM	1139	C	TYR	257	15.053	26.098	87.599	1.00	150.24
ATOM	1140	O	TYR	257	15.127	26.570	86.467	1.00	150.24
ATOM	1141	N	ASP	258	14.945	26.863	88.706	1.00	96.85
ATOM	1142	CA	ASP	258	14.800	28.282	88.571	1.00	96.85
ATOM	1143	CB	ASP	258	13.335	28.709	88.797	1.00	96.85
ATOM	1144	CG	ASP	258	13.113	30.119	88.281	1.00	96.85
ATOM	1145	OD1	ASP	258	14.109	30.883	88.199	1.00	96.85
ATOM	1146	OD2	ASP	258	11.941	30.448	87.958	1.00	96.85
ATOM	1147	C	ASP	258	15.644	28.937	89.624	1.00	96.85
ATOM	1148	O	ASP	258	15.412	28.753	90.817	1.00	96.85
ATOM	1149	N	SER	259	16.665	29.708	89.204	1.00	85.86
ATOM	1150	CA	SER	259	17.530	30.407	90.117	1.00	85.86
ATOM	1151	CB	SER	259	18.781	30.984	89.432	1.00	85.86
ATOM	1152	OG	SER	259	18.407	31.895	88.409	1.00	85.86
ATOM	1153	C	SER	259	16.768	31.549	90.718	1.00	85.86
ATOM	1154	O	SER	259	17.222	32.172	91.678	1.00	85.86
ATOM	1155	N	GLY	260	15.605	31.865	90.112	1.00	113.20
ATOM	1156	CA	GLY	260	14.706	32.930	90.474	1.00	113.20
ATOM	1157	C	GLY	260	14.045	32.686	91.792	1.00	113.20
ATOM	1158	O	GLY	260	13.764	33.636	92.515	1.00	113.20
ATOM	1159	N	GLY	261	13.720	31.424	92.130	1.00	86.72
ATOM	1160	CA	GLY	261	13.064	31.199	93.385	1.00	86.72
ATOM	1161	C	GLY	261	11.592	31.341	93.186	1.00	86.72
ATOM	1162	O	GLY	261	11.067	30.999	92.130	1.00	86.72
ATOM	1163	N	ASN	262	10.881	31.879	94.198	1.00	207.82
ATOM	1164	CA	ASN	262	9.456	31.925	94.083	1.00	207.82
ATOM	1165	CB	ASN	262	8.966	32.726	92.860	1.00	207.82
ATOM	1166	CG	ASN	262	9.258	34.208	93.079	1.00	207.82
ATOM	1167	OD1	ASN	262	9.119	34.718	94.189	1.00	207.82
ATOM	1168	ND2	ASN	262	9.670	34.916	91.994	1.00	207.82
ATOM	1169	C	ASN	262	9.035	30.503	93.904	1.00	207.82
ATOM	1170	O	ASN	262	8.251	30.184	93.012	1.00	207.82
ATOM	1171	N	ILE	263	9.571	29.630	94.787	1.00	193.31
ATOM	1172	CA	ILE	263	9.388	28.206	94.792	1.00	193.31
ATOM	1173	CB	ILE	263	9.688	27.587	96.127	1.00	193.31
ATOM	1174	CG2	ILE	263	8.780	28.259	97.166	1.00	193.31
ATOM	1175	CG1	ILE	263	9.539	26.058	96.070	1.00	193.31
ATOM	1176	CD1	ILE	263	10.598	25.377	95.202	1.00	193.31
ATOM	1177	C	ILE	263	7.983	27.869	94.442	1.00	193.31
ATOM	1178	O	ILE	263	7.026	28.491	94.897	1.00	193.31
ATOM	1179	N	PRO	264	7.860	26.906	93.580	1.00	100.94
ATOM	1180	CA	PRO	264	6.545	26.501	93.191	1.00	100.94
ATOM	1181	CD	PRO	264	8.797	26.817	92.472	1.00	100.94
ATOM	1182	CB	PRO	264	6.707	25.738	91.886	1.00	100.94
ATOM	1183	CG	PRO	264	7.964	26.365	91.262	1.00	100.94

ATOM	1184	C	PRO	264	5.889	25.722	94.276	1.00100.94
ATOM	1185	O	PRO	264	6.579	25.112	95.091	1.00100.94
ATOM	1186	N	THR	265	4.550	25.758	94.313	1.00232.51
ATOM	1187	CA	THR	265	3.808	25.043	95.300	1.00232.51
ATOM	1188	CB	THR	265	3.702	25.797	96.601	1.00232.51
ATOM	1189	OG1	THR	265	3.098	24.996	97.606	1.00232.51
ATOM	1190	CG2	THR	265	2.911	27.097	96.380	1.00232.51
ATOM	1191	C	THR	265	2.453	24.873	94.706	1.00232.51
ATOM	1192	O	THR	265	2.308	24.753	93.489	1.00232.51
ATOM	1193	N	GLU	266	1.419	24.847	95.556	1.00 72.96
ATOM	1194	CA	GLU	266	0.090	24.777	95.058	1.00 72.96
ATOM	1195	CB	GLU	266	-0.973	24.865	96.163	1.00 72.96
ATOM	1196	CG	GLU	266	-0.967	23.675	97.125	1.00 72.96
ATOM	1197	CD	GLU	266	-2.060	23.897	98.160	1.00 72.96
ATOM	1198	OE1	GLU	266	-3.191	24.275	97.757	1.00 72.96
ATOM	1199	OE2	GLU	266	-1.776	23.693	99.371	1.00 72.96
ATOM	1200	C	GLU	266	-0.048	26.011	94.241	1.00 72.96
ATOM	1201	O	GLU	266	-0.736	26.023	93.223	1.00 72.96
ATOM	1202	N	PHE	267	0.662	27.073	94.666	1.00 75.25
ATOM	1203	CA	PHE	267	0.549	28.365	94.062	1.00 75.25
ATOM	1204	CB	PHE	267	1.597	29.354	94.601	1.00 75.25
ATOM	1205	CG	PHE	267	1.160	30.739	94.260	1.00 75.25
ATOM	1206	CD1	PHE	267	0.265	31.380	95.082	1.00 75.25
ATOM	1207	CD2	PHE	267	1.637	31.400	93.151	1.00 75.25
ATOM	1208	CE1	PHE	267	-0.159	32.658	94.808	1.00 75.25
ATOM	1209	CE2	PHE	267	1.218	32.682	92.871	1.00 75.25
ATOM	1210	CZ	PHE	267	0.318	33.312	93.698	1.00 75.25
ATOM	1211	C	PHE	267	0.806	28.206	92.600	1.00 75.25
ATOM	1212	O	PHE	267	-0.005	28.644	91.785	1.00 75.25
ATOM	1213	N	HIS	268	1.926	27.569	92.209	1.00120.57
ATOM	1214	CA	HIS	268	2.071	27.374	90.801	1.00120.57
ATOM	1215	ND1	HIS	268	4.629	28.952	91.451	1.00120.57
ATOM	1216	CG	HIS	268	4.424	28.128	90.367	1.00120.57
ATOM	1217	CB	HIS	268	3.487	26.957	90.371	1.00120.57
ATOM	1218	NE2	HIS	268	5.893	29.745	89.801	1.00120.57
ATOM	1219	CD2	HIS	268	5.204	28.626	89.368	1.00120.57
ATOM	1220	CE1	HIS	268	5.514	29.902	91.057	1.00120.57
ATOM	1221	C	HIS	268	1.090	26.308	90.438	1.00120.57
ATOM	1222	O	HIS	268	0.964	25.311	91.144	1.00120.57
ATOM	1223	N	HIS	269	0.382	26.478	89.304	1.00285.66
ATOM	1224	CA	HIS	269	-0.638	25.533	88.947	1.00285.66
ATOM	1225	ND1	HIS	269	-1.508	22.985	86.957	1.00285.66
ATOM	1226	CG	HIS	269	-1.094	23.103	88.265	1.00285.66
ATOM	1227	CB	HIS	269	-0.088	24.110	88.745	1.00285.66
ATOM	1228	NE2	HIS	269	-2.589	21.420	88.112	1.00285.66
ATOM	1229	CD2	HIS	269	-1.765	22.141	88.955	1.00285.66
ATOM	1230	CE1	HIS	269	-2.403	21.963	86.922	1.00285.66
ATOM	1231	C	HIS	269	-1.663	25.496	90.041	1.00285.66
ATOM	1232	O	HIS	269	-2.053	24.430	90.513	1.00285.66
ATOM	1233	N	TYR	270	-2.135	26.680	90.480	1.00275.40
ATOM	1234	CA	TYR	270	-3.136	26.703	91.507	1.00275.40
ATOM	1235	CB	TYR	270	-2.831	27.685	92.652	1.00275.40
ATOM	1236	CG	TYR	270	-3.831	27.449	93.732	1.00275.40
ATOM	1237	CD1	TYR	270	-3.682	26.373	94.578	1.00275.40
ATOM	1238	CD2	TYR	270	-4.904	28.292	93.910	1.00275.40
ATOM	1239	CE1	TYR	270	-4.589	26.135	95.583	1.00275.40
ATOM	1240	CE2	TYR	270	-5.814	28.060	94.915	1.00275.40
ATOM	1241	CZ	TYR	270	-5.658	26.980	95.752	1.00275.40
ATOM	1242	OH	TYR	270	-6.591	26.743	96.784	1.00275.40
ATOM	1243	C	TYR	270	-4.386	27.189	90.857	1.00275.40
ATOM	1244	O	TYR	270	-4.368	28.183	90.132	1.00275.40
ATOM	1245	N	ASN	271	-5.513	26.488	91.082	1.00242.49
ATOM	1246	CA	ASN	271	-6.723	26.931	90.459	1.00242.49
ATOM	1247	CB	ASN	271	-7.903	25.953	90.624	1.00242.49
ATOM	1248	CG	ASN	271	-8.189	25.790	92.112	1.00242.49
ATOM	1249	OD1	ASN	271	-7.323	25.367	92.876	1.00242.49

ATOM	1250	ND2	ASN	271	-9.431	26.143	92.537	1.00242.49
ATOM	1251	C	ASN	271	-7.092	28.242	91.067	1.00242.49
ATOM	1252	O	ASN	271	-7.266	28.364	92.279	1.00242.49
ATOM	1253	N	ASN	272	-7.182	29.279	90.218	1.00289.61
ATOM	1254	CA	ASN	272	-7.544	30.581	90.681	1.00289.61
ATOM	1255	CB	ASN	272	-6.612	31.124	91.781	1.00289.61
ATOM	1256	CG	ASN	272	-5.168	31.036	91.298	1.00289.61
ATOM	1257	OD1	ASN	272	-4.407	30.209	91.794	1.00289.61
ATOM	1258	ND2	ASN	272	-4.774	31.887	90.314	1.00289.61
ATOM	1259	C	ASN	272	-7.490	31.497	89.508	1.00289.61
ATOM	1260	O	ASN	272	-6.959	31.145	88.456	1.00289.61
ATOM	1261	N	PHE	273	-8.071	32.701	89.651	1.00223.87
ATOM	1262	CA	PHE	273	-7.991	33.613	88.555	1.00223.87
ATOM	1263	CB	PHE	273	-9.254	34.480	88.413	1.00223.87
ATOM	1264	CG	PHE	273	-9.184	35.214	87.119	1.00223.87
ATOM	1265	CD1	PHE	273	-9.640	34.621	85.963	1.00223.87
ATOM	1266	CD2	PHE	273	-8.669	36.488	87.053	1.00223.87
ATOM	1267	CE1	PHE	273	-9.584	35.284	84.761	1.00223.87
ATOM	1268	CE2	PHE	273	-8.611	37.156	85.852	1.00223.87
ATOM	1269	CZ	PHE	273	-9.068	36.556	84.703	1.00223.87
ATOM	1270	C	PHE	273	-6.857	34.529	88.874	1.00223.87
ATOM	1271	O	PHE	273	-7.064	35.676	89.266	1.00223.87
ATOM	1272	N	TYR	274	-5.615	34.038	88.712	1.00256.35
ATOM	1273	CA	TYR	274	-4.475	34.866	88.967	1.00256.35
ATOM	1274	CB	TYR	274	-3.716	34.548	90.268	1.00256.35
ATOM	1275	CG	TYR	274	-4.554	34.961	91.425	1.00256.35
ATOM	1276	CD1	TYR	274	-5.525	34.132	91.933	1.00256.35
ATOM	1277	CD2	TYR	274	-4.353	36.193	92.007	1.00256.35
ATOM	1278	CE1	TYR	274	-6.290	34.526	93.006	1.00256.35
ATOM	1279	CE2	TYR	274	-5.113	36.595	93.079	1.00256.35
ATOM	1280	CZ	TYR	274	-6.080	35.760	93.580	1.00256.35
ATOM	1281	OH	TYR	274	-6.862	36.167	94.680	1.00256.35
ATOM	1282	C	TYR	274	-3.500	34.635	87.867	1.00256.35
ATOM	1283	O	TYR	274	-3.453	33.556	87.277	1.00256.35
ATOM	1284	N	PHE	275	-2.699	35.667	87.550	1.00303.44
ATOM	1285	CA	PHE	275	-1.698	35.480	86.550	1.00303.44
ATOM	1286	CB	PHE	275	-1.587	36.682	85.587	1.00303.44
ATOM	1287	CG	PHE	275	-1.447	37.922	86.400	1.00303.44
ATOM	1288	CD1	PHE	275	-2.552	38.467	87.016	1.00303.44
ATOM	1289	CD2	PHE	275	-0.233	38.554	86.539	1.00303.44
ATOM	1290	CE1	PHE	275	-2.442	39.612	87.769	1.00303.44
ATOM	1291	CE2	PHE	275	-0.116	39.698	87.293	1.00303.44
ATOM	1292	CZ	PHE	275	-1.222	40.231	87.910	1.00303.44
ATOM	1293	C	PHE	275	-0.395	35.232	87.247	1.00303.44
ATOM	1294	O	PHE	275	0.256	36.148	87.747	1.00303.44
ATOM	1295	N	TYR	276	-0.001	33.947	87.316	1.00249.15
ATOM	1296	CA	TYR	276	1.246	33.560	87.901	1.00249.15
ATOM	1297	CB	TYR	276	1.157	33.083	89.363	1.00249.15
ATOM	1298	CG	TYR	276	1.040	34.282	90.245	1.00249.15
ATOM	1299	CD1	TYR	276	-0.159	34.928	90.435	1.00249.15
ATOM	1300	CD2	TYR	276	2.158	34.758	90.891	1.00249.15
ATOM	1301	CE1	TYR	276	-0.240	36.029	91.256	1.00249.15
ATOM	1302	CE2	TYR	276	2.086	35.857	91.713	1.00249.15
ATOM	1303	CZ	TYR	276	0.887	36.497	91.894	1.00249.15
ATOM	1304	OH	TYR	276	0.813	37.627	92.736	1.00249.15
ATOM	1305	C	TYR	276	1.775	32.444	87.073	1.00249.15
ATOM	1306	O	TYR	276	1.053	31.868	86.260	1.00249.15
ATOM	1307	N	SER	277	3.071	32.124	87.243	1.00212.61
ATOM	1308	CA	SER	277	3.655	31.079	86.459	1.00212.61
ATOM	1309	CB	SER	277	5.186	31.022	86.551	1.00212.61
ATOM	1310	OG	SER	277	5.676	29.934	85.782	1.00212.61
ATOM	1311	C	SER	277	3.147	29.777	86.954	1.00212.61
ATOM	1312	O	SER	277	2.899	29.589	88.143	1.00212.61
ATOM	1313	N	PHE	278	2.950	28.826	86.033	1.00225.57
ATOM	1314	CA	PHE	278	2.565	27.549	86.524	1.00225.57
ATOM	1315	CB	PHE	278	1.482	26.853	85.681	1.00225.57

ATOM	1316	CG	PHE	278	0.264	27.710	85.688	1.00225.57
ATOM	1317	CD1	PHE	278	-0.538	27.793	86.804	1.00225.57
ATOM	1318	CD2	PHE	278	-0.085	28.421	84.564	1.00225.57
ATOM	1319	CE1	PHE	278	-1.663	28.585	86.801	1.00225.57
ATOM	1320	CE2	PHE	278	-1.209	29.212	84.555	1.00225.57
ATOM	1321	CZ	PHE	278	-2.000	29.297	85.676	1.00225.57
ATOM	1322	C	PHE	278	3.792	26.723	86.394	1.00225.57
ATOM	1323	O	PHE	278	4.126	26.285	85.296	1.00225.57
ATOM	1324	N	SER	279	4.509	26.495	87.509	1.00 63.44
ATOM	1325	CA	SER	279	5.684	25.695	87.383	1.00 63.44
ATOM	1326	CB	SER	279	6.414	25.459	88.712	1.00 63.44
ATOM	1327	OG	SER	279	5.673	24.541	89.502	1.00 63.44
ATOM	1328	C	SER	279	5.183	24.367	86.941	1.00 63.44
ATOM	1329	O	SER	279	5.805	23.687	86.126	1.00 63.44
ATOM	1330	N	ASP	280	4.011	23.979	87.478	1.00 78.81
ATOM	1331	CA	ASP	280	3.420	22.723	87.134	1.00 78.81
ATOM	1332	CB	ASP	280	2.171	22.387	87.972	1.00 78.81
ATOM	1333	CG	ASP	280	1.793	20.921	87.778	1.00 78.81
ATOM	1334	OD1	ASP	280	2.351	20.272	86.853	1.00 78.81
ATOM	1335	OD2	ASP	280	0.932	20.429	88.557	1.00 78.81
ATOM	1336	C	ASP	280	3.030	22.764	85.691	1.00 78.81
ATOM	1337	O	ASP	280	3.170	21.773	84.979	1.00 78.81
ATOM	1338	N	GLY	281	2.542	23.920	85.202	1.00 25.80
ATOM	1339	CA	GLY	281	2.096	23.971	83.838	1.00 25.80
ATOM	1340	C	GLY	281	3.249	23.655	82.943	1.00 25.80
ATOM	1341	O	GLY	281	3.109	22.929	81.960	1.00 25.80
ATOM	1342	N	PHE	282	4.428	24.220	83.251	1.00106.36
ATOM	1343	CA	PHE	282	5.584	23.975	82.445	1.00106.36
ATOM	1344	CB	PHE	282	6.742	24.933	82.760	1.00106.36
ATOM	1345	CG	PHE	282	6.193	26.279	82.417	1.00106.36
ATOM	1346	CD1	PHE	282	5.939	26.615	81.107	1.00106.36
ATOM	1347	CD2	PHE	282	5.873	27.191	83.396	1.00106.36
ATOM	1348	CE1	PHE	282	5.420	27.847	80.783	1.00106.36
ATOM	1349	CE2	PHE	282	5.354	28.426	83.081	1.00106.36
ATOM	1350	CZ	PHE	282	5.129	28.759	81.769	1.00106.36
ATOM	1351	C	PHE	282	5.994	22.546	82.609	1.00106.36
ATOM	1352	O	PHE	282	6.395	21.879	81.655	1.00106.36
ATOM	1353	N	ASN	283	5.894	22.022	83.837	1.00 71.40
ATOM	1354	CA	ASN	283	6.291	20.668	84.067	1.00 71.40
ATOM	1355	CB	ASN	283	6.129	20.284	85.548	1.00 71.40
ATOM	1356	CG	ASN	283	7.090	19.149	85.868	1.00 71.40
ATOM	1357	OD1	ASN	283	7.211	18.171	85.133	1.00 71.40
ATOM	1358	ND2	ASN	283	7.820	19.297	87.008	1.00 71.40
ATOM	1359	C	ASN	283	5.407	19.779	83.242	1.00 71.40
ATOM	1360	O	ASN	283	5.874	18.832	82.610	1.00 71.40
ATOM	1361	N	THR	284	4.096	20.080	83.210	1.00 44.86
ATOM	1362	CA	THR	284	3.160	19.258	82.495	1.00 44.86
ATOM	1363	CB	THR	284	1.723	19.648	82.719	1.00 44.86
ATOM	1364	OG1	THR	284	1.471	20.953	82.223	1.00 44.86
ATOM	1365	CG2	THR	284	1.431	19.587	84.228	1.00 44.86
ATOM	1366	C	THR	284	3.429	19.312	81.021	1.00 44.86
ATOM	1367	O	THR	284	3.338	18.295	80.336	1.00 44.86
ATOM	1368	N	ASN	285	3.767	20.490	80.464	1.00113.18
ATOM	1369	CA	ASN	285	3.937	20.471	79.040	1.00113.18
ATOM	1370	CB	ASN	285	4.035	21.849	78.339	1.00113.18
ATOM	1371	CG	ASN	285	5.264	22.649	78.742	1.00113.18
ATOM	1372	OD1	ASN	285	5.305	23.238	79.820	1.00113.18
ATOM	1373	ND2	ASN	285	6.279	22.708	77.839	1.00113.18
ATOM	1374	C	ASN	285	5.103	19.610	78.677	1.00113.18
ATOM	1375	O	ASN	285	5.067	18.915	77.663	1.00113.18
ATOM	1376	N	HIS	286	6.174	19.630	79.493	1.00 90.92
ATOM	1377	CA	HIS	286	7.325	18.828	79.199	1.00 90.92
ATOM	1378	ND1	HIS	286	8.719	21.730	80.154	1.00 90.92
ATOM	1379	CG	HIS	286	9.117	20.516	79.637	1.00 90.92
ATOM	1380	CB	HIS	286	8.553	19.186	80.056	1.00 90.92
ATOM	1381	NE2	HIS	286	10.242	22.175	78.595	1.00 90.92

ATOM	1382	CD2	HIS	286	10.049	20.808	78.687	1.00	90.92
ATOM	1383	CE1	HIS	286	9.423	22.686	79.496	1.00	90.92
ATOM	1384	C	HIS	286	6.981	17.374	79.330	1.00	90.92
ATOM	1385	O	HIS	286	7.465	16.548	78.558	1.00	90.92
ATOM	1386	N	ARG	287	6.138	17.004	80.312	1.00	141.18
ATOM	1387	CA	ARG	287	5.788	15.618	80.444	1.00	141.18
ATOM	1388	CB	ARG	287	4.986	15.299	81.722	1.00	141.18
ATOM	1389	CG	ARG	287	3.659	16.045	81.861	1.00	141.18
ATOM	1390	CD	ARG	287	3.010	15.899	83.240	1.00	141.18
ATOM	1391	NE	ARG	287	2.505	14.503	83.359	1.00	141.18
ATOM	1392	CZ	ARG	287	2.130	14.010	84.576	1.00	141.18
ATOM	1393	NH1	ARG	287	2.255	14.780	85.697	1.00	141.18
ATOM	1394	NH2	ARG	287	1.628	12.745	84.674	1.00	141.18
ATOM	1395	C	ARG	287	5.012	15.190	79.231	1.00	141.18
ATOM	1396	O	ARG	287	5.196	14.084	78.724	1.00	141.18
ATOM	1397	N	HIS	288	4.133	16.070	78.717	1.00	43.21
ATOM	1398	CA	HIS	288	3.338	15.721	77.574	1.00	43.21
ATOM	1399	ND1	HIS	288	1.012	17.652	79.158	1.00	43.21
ATOM	1400	CG	HIS	288	1.124	16.884	78.021	1.00	43.21
ATOM	1401	CB	HIS	288	2.343	16.816	77.150	1.00	43.21
ATOM	1402	NE2	HIS	288	-0.925	16.585	78.920	1.00	43.21
ATOM	1403	CD2	HIS	288	-0.068	16.239	77.890	1.00	43.21
ATOM	1404	CE1	HIS	288	-0.231	17.436	79.655	1.00	43.21
ATOM	1405	C	HIS	288	4.234	15.466	76.408	1.00	43.21
ATOM	1406	O	HIS	288	4.005	14.539	75.632	1.00	43.21
ATOM	1407	N	SER	289	5.288	16.283	76.253	1.00	89.65
ATOM	1408	CA	SER	289	6.140	16.122	75.117	1.00	89.65
ATOM	1409	CB	SER	289	7.274	17.163	75.059	1.00	89.65
ATOM	1410	OG	SER	289	8.195	16.969	76.123	1.00	89.65
ATOM	1411	C	SER	289	6.756	14.760	75.151	1.00	89.65
ATOM	1412	O	SER	289	6.803	14.067	74.135	1.00	89.65
ATOM	1413	N	VAL	290	7.217	14.320	76.336	1.00	99.64
ATOM	1414	CA	VAL	290	7.893	13.056	76.415	1.00	99.64
ATOM	1415	CB	VAL	290	8.469	12.758	77.774	1.00	99.64
ATOM	1416	CG1	VAL	290	7.346	12.382	78.758	1.00	99.64
ATOM	1417	CG2	VAL	290	9.536	11.666	77.605	1.00	99.64
ATOM	1418	C	VAL	290	6.953	11.956	76.037	1.00	99.64
ATOM	1419	O	VAL	290	7.327	11.026	75.320	1.00	99.64
ATOM	1420	N	LEU	291	5.691	12.036	76.497	1.00	46.15
ATOM	1421	CA	LEU	291	4.779	10.965	76.218	1.00	46.15
ATOM	1422	CB	LEU	291	3.395	11.206	76.843	1.00	46.15
ATOM	1423	CG	LEU	291	3.406	11.257	78.381	1.00	46.15
ATOM	1424	CD2	LEU	291	4.089	10.018	78.976	1.00	46.15
ATOM	1425	CD1	LEU	291	1.993	11.495	78.941	1.00	46.15
ATOM	1426	C	LEU	291	4.587	10.835	74.738	1.00	46.15
ATOM	1427	O	LEU	291	4.734	9.747	74.188	1.00	46.15
ATOM	1428	N	ASP	292	4.279	11.942	74.041	1.00	47.77
ATOM	1429	CA	ASP	292	4.022	11.838	72.632	1.00	47.77
ATOM	1430	CB	ASP	292	3.490	13.142	72.008	1.00	47.77
ATOM	1431	CG	ASP	292	2.051	13.321	72.471	1.00	47.77
ATOM	1432	OD1	ASP	292	1.653	12.617	73.437	1.00	47.77
ATOM	1433	OD2	ASP	292	1.328	14.153	71.860	1.00	47.77
ATOM	1434	C	ASP	292	5.268	11.458	71.892	1.00	47.77
ATOM	1435	O	ASP	292	5.248	10.591	71.021	1.00	47.77
ATOM	1436	N	ASN	293	6.401	12.074	72.258	1.00	70.18
ATOM	1437	CA	ASN	293	7.631	11.877	71.552	1.00	70.18
ATOM	1438	CB	ASN	293	8.800	12.681	72.147	1.00	70.18
ATOM	1439	CG	ASN	293	8.565	14.161	71.889	1.00	70.18
ATOM	1440	OD1	ASN	293	8.744	14.990	72.780	1.00	70.18
ATOM	1441	ND2	ASN	293	8.158	14.506	70.638	1.00	70.18
ATOM	1442	C	ASN	293	8.041	10.445	71.641	1.00	70.18
ATOM	1443	O	ASN	293	8.595	9.890	70.694	1.00	70.18
ATOM	1444	N	THR	294	7.720	9.801	72.774	1.00	170.59
ATOM	1445	CA	THR	294	8.211	8.503	73.129	1.00	170.59
ATOM	1446	CB	THR	294	7.949	8.123	74.555	1.00	170.59
ATOM	1447	OG1	THR	294	8.805	7.051	74.907	1.00	170.59

ATOM	1448	CG2	THR	294	6.491	7.702	74.748	1.00170.59
ATOM	1449	C	THR	294	7.757	7.433	72.190	1.00170.59
ATOM	1450	O	THR	294	8.237	6.304	72.282	1.00170.59
ATOM	1451	N	ASN	295	6.774	7.731	71.317	1.00213.44
ATOM	1452	CA	ASN	295	6.301	6.773	70.350	1.00213.44
ATOM	1453	CB	ASN	295	5.514	7.401	69.190	1.00213.44
ATOM	1454	CG	ASN	295	5.078	6.279	68.254	1.00213.44
ATOM	1455	OD1	ASN	295	5.051	6.437	67.033	1.00213.44
ATOM	1456	ND2	ASN	295	4.729	5.109	68.851	1.00213.44
ATOM	1457	C	ASN	295	7.468	6.132	69.673	1.00213.44
ATOM	1458	O	ASN	295	8.429	6.801	69.292	1.00213.44
ATOM	1459	N	CYS	296	7.412	4.792	69.533	1.00101.49
ATOM	1460	CA	CYS	296	8.454	4.083	68.851	1.00101.49
ATOM	1461	CB	CYS	296	8.568	2.604	69.264	1.00101.49
ATOM	1462	SG	CYS	296	9.930	1.754	68.413	1.00101.49
ATOM	1463	C	CYS	296	8.104	4.134	67.402	1.00101.49
ATOM	1464	O	CYS	296	6.929	4.186	67.044	1.00101.49
ATOM	1465	N	ASP	297	9.119	4.140	66.521	1.00198.12
ATOM	1466	CA	ASP	297	8.815	4.244	65.127	1.00198.12
ATOM	1467	CB	ASP	297	10.019	4.633	64.246	1.00198.12
ATOM	1468	CG	ASP	297	11.101	3.567	64.361	1.00198.12
ATOM	1469	OD1	ASP	297	11.108	2.835	65.387	1.00198.12
ATOM	1470	OD2	ASP	297	11.935	3.473	63.422	1.00198.12
ATOM	1471	C	ASP	297	8.269	2.946	64.633	1.00198.12
ATOM	1472	O	ASP	297	8.807	1.874	64.906	1.00198.12
ATOM	1473	N	ILE	298	7.142	3.027	63.905	1.00116.45
ATOM	1474	CA	ILE	298	6.549	1.879	63.287	1.00116.45
ATOM	1475	CB	ILE	298	5.264	1.433	63.922	1.00116.45
ATOM	1476	CG2	ILE	298	4.663	0.329	63.035	1.00116.45
ATOM	1477	CG1	ILE	298	5.513	0.971	65.367	1.00116.45
ATOM	1478	CD1	ILE	298	6.452	-0.232	65.460	1.00116.45
ATOM	1479	C	ILE	298	6.254	2.310	61.889	1.00116.45
ATOM	1480	O	ILE	298	5.966	3.481	61.648	1.00116.45
ATOM	1481	N	ASP	299	6.333	1.387	60.914	1.00128.04
ATOM	1482	CA	ASP	299	6.120	1.839	59.573	1.00128.04
ATOM	1483	CB	ASP	299	6.821	0.987	58.505	1.00128.04
ATOM	1484	CG	ASP	299	8.305	1.313	58.560	1.00128.04
ATOM	1485	OD1	ASP	299	8.641	2.446	58.996	1.00128.04
ATOM	1486	OD2	ASP	299	9.123	0.440	58.162	1.00128.04
ATOM	1487	C	ASP	299	4.663	1.841	59.266	1.00128.04
ATOM	1488	O	ASP	299	4.075	0.803	58.966	1.00128.04
ATOM	1489	N	VAL	300	4.045	3.036	59.358	1.00 95.52
ATOM	1490	CA	VAL	300	2.676	3.219	58.980	1.00 95.52
ATOM	1491	CB	VAL	300	1.693	3.088	60.109	1.00 95.52
ATOM	1492	CG1	VAL	300	1.938	4.223	61.112	1.00 95.52
ATOM	1493	CG2	VAL	300	0.271	3.068	59.522	1.00 95.52
ATOM	1494	C	VAL	300	2.586	4.610	58.444	1.00 95.52
ATOM	1495	O	VAL	300	3.372	5.482	58.813	1.00 95.52
ATOM	1496	N	LEU	301	1.639	4.850	57.521	1.00134.46
ATOM	1497	CA	LEU	301	1.513	6.160	56.958	1.00134.46
ATOM	1498	CB	LEU	301	0.478	6.198	55.812	1.00134.46
ATOM	1499	CG	LEU	301	0.286	7.570	55.135	1.00134.46
ATOM	1500	CD2	LEU	301	1.623	8.122	54.624	1.00134.46
ATOM	1501	CD1	LEU	301	-0.477	8.575	56.022	1.00134.46
ATOM	1502	C	LEU	301	1.070	7.096	58.034	1.00134.46
ATOM	1503	O	LEU	301	1.647	8.167	58.210	1.00134.46
ATOM	1504	N	PHE	302	0.051	6.683	58.809	1.00199.62
ATOM	1505	CA	PHE	302	-0.511	7.566	59.788	1.00199.62
ATOM	1506	CB	PHE	302	-1.706	6.990	60.564	1.00199.62
ATOM	1507	CG	PHE	302	-2.899	7.050	59.679	1.00199.62
ATOM	1508	CD1	PHE	302	-3.141	6.069	58.746	1.00199.62
ATOM	1509	CD2	PHE	302	-3.783	8.099	59.792	1.00199.62
ATOM	1510	CE1	PHE	302	-4.251	6.139	57.938	1.00199.62
ATOM	1511	CE2	PHE	302	-4.894	8.174	58.987	1.00199.62
ATOM	1512	CZ	PHE	302	-5.128	7.192	58.057	1.00199.62
ATOM	1513	C	PHE	302	0.527	7.940	60.779	1.00199.62

ATOM	1514	O	PHE	302	1.359	7.129	61.181	1.00199.62
ATOM	1515	N	ARG	303	0.492	9.225	61.173	1.00292.70
ATOM	1516	CA	ARG	303	1.403	9.730	62.147	1.00292.70
ATOM	1517	CB	ARG	303	1.470	11.268	62.135	1.00292.70
ATOM	1518	CG	ARG	303	1.638	11.837	60.722	1.00292.70
ATOM	1519	CD	ARG	303	2.555	11.002	59.823	1.00292.70
ATOM	1520	NE	ARG	303	3.962	11.304	60.204	1.00292.70
ATOM	1521	CZ	ARG	303	4.645	12.265	59.519	1.00292.70
ATOM	1522	NH1	ARG	303	4.042	12.911	58.477	1.00292.70
ATOM	1523	NH2	ARG	303	5.926	12.578	59.870	1.00292.70
ATOM	1524	C	ARG	303	0.840	9.292	63.457	1.00292.70
ATOM	1525	O	ARG	303	-0.374	9.323	63.656	1.00292.70
ATOM	1526	N	PHE	304	1.696	8.828	64.386	1.00364.50
ATOM	1527	CA	PHE	304	1.136	8.409	65.635	1.00364.50
ATOM	1528	CB	PHE	304	0.619	6.960	65.616	1.00364.50
ATOM	1529	CG	PHE	304	1.788	6.043	65.500	1.00364.50
ATOM	1530	CD1	PHE	304	2.484	5.926	64.319	1.00364.50
ATOM	1531	CD2	PHE	304	2.179	5.282	66.579	1.00364.50
ATOM	1532	CE1	PHE	304	3.561	5.076	64.219	1.00364.50
ATOM	1533	CE2	PHE	304	3.252	4.430	66.486	1.00364.50
ATOM	1534	CZ	PHE	304	3.948	4.329	65.305	1.00364.50
ATOM	1535	C	PHE	304	2.211	8.484	66.662	1.00364.50
ATOM	1536	O	PHE	304	3.395	8.553	66.337	1.00364.50
ATOM	1537	N	PHE	305	1.813	8.500	67.948	1.00306.52
ATOM	1538	CA	PHE	305	2.791	8.519	68.989	1.00306.52
ATOM	1539	CB	PHE	305	2.949	9.878	69.683	1.00306.52
ATOM	1540	CG	PHE	305	3.405	10.843	68.644	1.00306.52
ATOM	1541	CD1	PHE	305	4.742	10.999	68.357	1.00306.52
ATOM	1542	CD2	PHE	305	2.483	11.584	67.941	1.00306.52
ATOM	1543	CE1	PHE	305	5.151	11.892	67.394	1.00306.52
ATOM	1544	CE2	PHE	305	2.884	12.476	66.980	1.00306.52
ATOM	1545	CZ	PHE	305	4.222	12.633	66.704	1.00306.52
ATOM	1546	C	PHE	305	2.345	7.530	70.011	1.00306.52
ATOM	1547	O	PHE	305	1.177	7.147	70.053	1.00306.52
ATOM	1548	N	GLU	306	3.284	7.068	70.857	1.00342.97
ATOM	1549	CA	GLU	306	2.943	6.091	71.839	1.00342.97
ATOM	1550	CB	GLU	306	3.653	4.743	71.637	1.00342.97
ATOM	1551	CG	GLU	306	3.154	3.659	72.591	1.00342.97
ATOM	1552	CD	GLU	306	1.759	3.263	72.136	1.00342.97
ATOM	1553	OE1	GLU	306	0.911	4.177	71.957	1.00342.97
ATOM	1554	OE2	GLU	306	1.526	2.040	71.953	1.00342.97
ATOM	1555	C	GLU	306	3.403	6.632	73.134	1.00342.97
ATOM	1556	O	GLU	306	4.288	7.477	73.156	1.00342.97
ATOM	1557	N	CYS	307	2.782	6.194	74.242	1.00213.88
ATOM	1558	CA	CYS	307	3.216	6.642	75.528	1.00213.88
ATOM	1559	CB	CYS	307	2.049	6.937	76.485	1.00213.88
ATOM	1560	SG	CYS	307	2.584	7.483	78.133	1.00213.88
ATOM	1561	C	CYS	307	3.980	5.518	76.139	1.00213.88
ATOM	1562	O	CYS	307	3.536	4.924	77.120	1.00213.88
ATOM	1563	N	THR	308	5.153	5.179	75.571	1.00 57.58
ATOM	1564	CA	THR	308	5.880	4.113	76.186	1.00 57.58
ATOM	1565	CB	THR	308	7.029	3.587	75.371	1.00 57.58
ATOM	1566	OG1	THR	308	8.022	4.581	75.190	1.00 57.58
ATOM	1567	CG2	THR	308	6.482	3.124	74.008	1.00 57.58
ATOM	1568	C	THR	308	6.367	4.607	77.510	1.00 57.58
ATOM	1569	O	THR	308	6.287	3.892	78.508	1.00 57.58
ATOM	1570	N	PHE	309	6.869	5.859	77.568	1.00 67.82
ATOM	1571	CA	PHE	309	7.312	6.349	78.840	1.00 67.82
ATOM	1572	CB	PHE	309	8.826	6.214	79.115	1.00 67.82
ATOM	1573	CG	PHE	309	9.636	6.893	78.063	1.00 67.82
ATOM	1574	CD1	PHE	309	9.635	8.263	77.934	1.00 67.82
ATOM	1575	CD2	PHE	309	10.439	6.147	77.228	1.00 67.82
ATOM	1576	CE1	PHE	309	10.399	8.871	76.964	1.00 67.82
ATOM	1577	CE2	PHE	309	11.207	6.748	76.258	1.00 67.82
ATOM	1578	CZ	PHE	309	11.184	8.116	76.125	1.00 67.82
ATOM	1579	C	PHE	309	6.919	7.779	79.026	1.00 67.82

ATOM	1580	O	PHE	309	6.449	8.450	78.106	1.00	67.82
ATOM	1581	N	GLY	310	7.095	8.266	80.272	1.00	35.84
ATOM	1582	CA	GLY	310	6.795	9.622	80.629	1.00	35.84
ATOM	1583	C	GLY	310	5.596	9.675	81.529	1.00	35.84
ATOM	1584	O	GLY	310	5.433	10.622	82.292	1.00	35.84
ATOM	1585	N	ALA	311	4.715	8.665	81.494	1.00	33.99
ATOM	1586	CA	ALA	311	3.551	8.737	82.334	1.00	33.99
ATOM	1587	CB	ALA	311	2.593	7.553	82.123	1.00	33.99
ATOM	1588	C	ALA	311	3.963	8.717	83.777	1.00	33.99
ATOM	1589	O	ALA	311	3.420	9.452	84.601	1.00	33.99
ATOM	1590	N	LYS	312	4.942	7.855	84.105	1.00	97.86
ATOM	1591	CA	LYS	312	5.431	7.608	85.435	1.00	97.86
ATOM	1592	CB	LYS	312	6.471	6.478	85.476	1.00	97.86
ATOM	1593	CG	LYS	312	7.054	6.237	86.870	1.00	97.86
ATOM	1594	CD	LYS	312	8.056	5.083	86.912	1.00	97.86
ATOM	1595	CE	LYS	312	8.821	4.978	88.232	1.00	97.86
ATOM	1596	NZ	LYS	312	9.860	3.929	88.129	1.00	97.86
ATOM	1597	C	LYS	312	6.119	8.801	86.022	1.00	97.86
ATOM	1598	O	LYS	312	6.024	9.029	87.226	1.00	97.86
ATOM	1599	N	ILE	313	6.830	9.577	85.180	1.00	184.69
ATOM	1600	CA	ILE	313	7.702	10.644	85.599	1.00	184.69
ATOM	1601	CB	ILE	313	8.110	11.557	84.467	1.00	184.69
ATOM	1602	CG2	ILE	313	6.838	12.252	83.963	1.00	184.69
ATOM	1603	CG1	ILE	313	9.144	12.612	84.889	1.00	184.69
ATOM	1604	CD1	ILE	313	8.499	13.804	85.601	1.00	184.69
ATOM	1605	C	ILE	313	7.132	11.465	86.706	1.00	184.69
ATOM	1606	O	ILE	313	5.961	11.845	86.706	1.00	184.69
ATOM	1607	N	GLY	314	7.997	11.749	87.704	1.00	35.77
ATOM	1608	CA	GLY	314	7.623	12.563	88.821	1.00	35.77
ATOM	1609	C	GLY	314	8.114	13.944	88.534	1.00	35.77
ATOM	1610	O	GLY	314	9.280	14.149	88.197	1.00	35.77
ATOM	1611	N	CYS	315	7.215	14.934	88.701	1.00	51.27
ATOM	1612	CA	CYS	315	7.513	16.300	88.388	1.00	51.27
ATOM	1613	CB	CYS	315	6.266	17.071	87.920	1.00	51.27
ATOM	1614	SG	CYS	315	5.480	16.313	86.465	1.00	51.27
ATOM	1615	C	CYS	315	7.996	16.961	89.641	1.00	51.27
ATOM	1616	O	CYS	315	7.345	16.879	90.680	1.00	51.27
ATOM	1617	N	ILE	316	9.167	17.633	89.588	1.00	113.12
ATOM	1618	CA	ILE	316	9.648	18.251	90.791	1.00	113.12
ATOM	1619	CB	ILE	316	10.793	17.532	91.440	1.00	113.12
ATOM	1620	CG2	ILE	316	10.331	16.122	91.832	1.00	113.12
ATOM	1621	CG1	ILE	316	12.019	17.553	90.513	1.00	113.12
ATOM	1622	CD1	ILE	316	13.308	17.116	91.205	1.00	113.12
ATOM	1623	C	ILE	316	10.183	19.612	90.486	1.00	113.12
ATOM	1624	O	ILE	316	10.554	19.915	89.352	1.00	113.12
ATOM	1625	N	ASN	317	10.206	20.482	91.518	1.00	92.47
ATOM	1626	CA	ASN	317	10.838	21.761	91.377	1.00	92.47
ATOM	1627	CB	ASN	317	10.161	22.905	92.150	1.00	92.47
ATOM	1628	CG	ASN	317	10.876	24.189	91.747	1.00	92.47
ATOM	1629	OD1	ASN	317	10.384	24.950	90.915	1.00	92.47
ATOM	1630	ND2	ASN	317	12.075	24.434	92.341	1.00	92.47
ATOM	1631	C	ASN	317	12.201	21.563	91.963	1.00	92.47
ATOM	1632	O	ASN	317	12.334	21.185	93.126	1.00	92.47
ATOM	1633	N	VAL	318	13.250	21.804	91.152	1.00	256.82
ATOM	1634	CA	VAL	318	14.596	21.482	91.537	1.00	256.82
ATOM	1635	CB	VAL	318	15.623	21.610	90.449	1.00	256.82
ATOM	1636	CG1	VAL	318	15.173	20.771	89.246	1.00	256.82
ATOM	1637	CG2	VAL	318	15.914	23.088	90.171	1.00	256.82
ATOM	1638	C	VAL	318	15.119	22.296	92.674	1.00	256.82
ATOM	1639	O	VAL	318	15.781	21.736	93.533	1.00	256.82
ATOM	1640	N	GLU	319	14.886	23.621	92.735	1.00	148.90
ATOM	1641	CA	GLU	319	15.486	24.392	93.794	1.00	148.90
ATOM	1642	CB	GLU	319	15.190	23.832	95.199	1.00	148.90
ATOM	1643	CG	GLU	319	13.709	23.927	95.574	1.00	148.90
ATOM	1644	CD	GLU	319	13.460	23.130	96.851	1.00	148.90
ATOM	1645	OE1	GLU	319	13.574	21.877	96.798	1.00	148.90

ATOM	1646	OE2	GLU	319	13.148	23.765	97.892	1.00148.90
ATOM	1647	C	GLU	319	16.978	24.456	93.572	1.00148.90
ATOM	1648	O	GLU	319	17.639	23.445	93.335	1.00148.90
ATOM	1649	N	VAL	320	17.541	25.684	93.630	1.00135.20
ATOM	1650	CA	VAL	320	18.939	25.956	93.415	1.00135.20
ATOM	1651	CB	VAL	320	19.301	26.059	91.973	1.00135.20
ATOM	1652	CG1	VAL	320	19.047	24.688	91.331	1.00135.20
ATOM	1653	CG2	VAL	320	18.490	27.217	91.365	1.00135.20
ATOM	1654	C	VAL	320	19.198	27.310	94.009	1.00135.20
ATOM	1655	O	VAL	320	18.335	27.853	94.695	1.00135.20
ATOM	1656	N	ASN	321	20.400	27.891	93.786	1.00 93.84
ATOM	1657	CA	ASN	321	20.666	29.190	94.359	1.00 93.84
ATOM	1658	CB	ASN	321	21.812	29.200	95.388	1.00 93.84
ATOM	1659	CG	ASN	321	21.303	28.624	96.706	1.00 93.84
ATOM	1660	OD1	ASN	321	20.829	27.491	96.775	1.00 93.84
ATOM	1661	ND2	ASN	321	21.410	29.436	97.792	1.00 93.84
ATOM	1662	C	ASN	321	21.035	30.190	93.295	1.00 93.84
ATOM	1663	O	ASN	321	21.555	29.809	92.247	1.00 93.84
ATOM	1664	N	GLN	322	20.714	31.494	93.532	1.00148.83
ATOM	1665	CA	GLN	322	21.092	32.602	92.679	1.00148.83
ATOM	1666	CB	GLN	322	20.070	32.903	91.568	1.00148.83
ATOM	1667	CG	GLN	322	20.478	34.077	90.674	1.00148.83
ATOM	1668	CD	GLN	322	19.349	34.341	89.685	1.00148.83
ATOM	1669	OE1	GLN	322	18.191	34.027	89.953	1.00148.83
ATOM	1670	NE2	GLN	322	19.687	34.933	88.508	1.00148.83
ATOM	1671	C	GLN	322	21.136	33.844	93.533	1.00148.83
ATOM	1672	O	GLN	322	20.094	34.357	93.940	1.00148.83
ATOM	1673	N	LEU	323	22.347	34.356	93.837	1.00 98.47
ATOM	1674	CA	LEU	323	22.494	35.530	94.658	1.00 98.47
ATOM	1675	CB	LEU	323	23.936	35.739	95.155	1.00 98.47
ATOM	1676	CG	LEU	323	24.402	34.643	96.134	1.00 98.47
ATOM	1677	CD2	LEU	323	25.708	35.041	96.839	1.00 98.47
ATOM	1678	CD1	LEU	323	24.481	33.271	95.446	1.00 98.47
ATOM	1679	C	LEU	323	22.063	36.788	93.956	1.00 98.47
ATOM	1680	O	LEU	323	21.361	37.611	94.542	1.00 98.47
ATOM	1681	N	LEU	324	22.461	36.971	92.679	1.00102.11
ATOM	1682	CA	LEU	324	22.197	38.215	91.998	1.00102.11
ATOM	1683	CB	LEU	324	23.396	38.736	91.189	1.00102.11
ATOM	1684	CG	LEU	324	24.622	39.078	92.054	1.00102.11
ATOM	1685	CD2	LEU	324	25.679	39.847	91.245	1.00102.11
ATOM	1686	CD1	LEU	324	25.189	37.824	92.735	1.00102.11
ATOM	1687	C	LEU	324	21.072	38.030	91.029	1.00102.11
ATOM	1688	O	LEU	324	20.724	36.910	90.663	1.00102.11
ATOM	1689	N	GLU	325	20.431	39.156	90.650	1.00108.72
ATOM	1690	CA	GLU	325	19.301	39.181	89.763	1.00108.72
ATOM	1691	CB	GLU	325	18.537	40.512	89.835	1.00108.72
ATOM	1692	CG	GLU	325	17.134	40.441	89.235	1.00108.72
ATOM	1693	CD	GLU	325	16.380	41.683	89.684	1.00108.72
ATOM	1694	OE1	GLU	325	17.036	42.746	89.850	1.00108.72
ATOM	1695	OE2	GLU	325	15.137	41.585	89.868	1.00108.72
ATOM	1696	C	GLU	325	19.644	38.919	88.314	1.00108.72
ATOM	1697	O	GLU	325	18.895	38.230	87.627	1.00108.72
ATOM	1698	N	SER	326	20.757	39.493	87.804	1.00114.97
ATOM	1699	CA	SER	326	21.134	39.467	86.406	1.00114.97
ATOM	1700	CB	SER	326	22.097	40.613	86.069	1.00114.97
ATOM	1701	OG	SER	326	21.438	41.862	86.241	1.00114.97
ATOM	1702	C	SER	326	21.748	38.170	85.936	1.00114.97
ATOM	1703	O	SER	326	21.853	37.921	84.736	1.00114.97
ATOM	1704	N	GLU	327	22.181	37.316	86.870	1.00104.93
ATOM	1705	CA	GLU	327	22.890	36.083	86.653	1.00104.93
ATOM	1706	CB	GLU	327	23.539	35.575	87.950	1.00104.93
ATOM	1707	CG	GLU	327	24.691	36.466	88.432	1.00104.93
ATOM	1708	CD	GLU	327	25.159	35.965	89.792	1.00104.93
ATOM	1709	OE1	GLU	327	24.287	35.748	90.677	1.00104.93
ATOM	1710	OE2	GLU	327	26.396	35.797	89.967	1.00104.93
ATOM	1711	C	GLU	327	22.049	34.976	86.057	1.00104.93

ATOM	1712	O	GLU	327	22.597	33.944	85.674	1.00104.93
ATOM	1713	N	CYS	328	20.712	35.125	85.963	1.00 88.66
ATOM	1714	CA	CYS	328	19.835	34.019	85.648	1.00 88.66
ATOM	1715	CB	CYS	328	18.367	34.439	85.426	1.00 88.66
ATOM	1716	SG	CYS	328	18.128	35.433	83.921	1.00 88.66
ATOM	1717	C	CYS	328	20.255	33.241	84.426	1.00 88.66
ATOM	1718	O	CYS	328	20.216	32.013	84.459	1.00 88.66
ATOM	1719	N	GLY	329	20.650	33.889	83.316	1.00 48.60
ATOM	1720	CA	GLY	329	21.026	33.129	82.149	1.00 48.60
ATOM	1721	C	GLY	329	22.236	32.301	82.465	1.00 48.60
ATOM	1722	O	GLY	329	22.398	31.182	81.981	1.00 48.60
ATOM	1723	N	MET	330	23.148	32.862	83.269	1.00133.02
ATOM	1724	CA	MET	330	24.370	32.223	83.650	1.00133.02
ATOM	1725	CB	MET	330	25.183	33.184	84.533	1.00133.02
ATOM	1726	CG	MET	330	26.681	32.964	84.459	1.00133.02
ATOM	1727	SD	MET	330	27.124	31.237	84.706	1.00133.02
ATOM	1728	CE	MET	330	26.458	31.100	86.390	1.00133.02
ATOM	1729	C	MET	330	24.027	30.990	84.449	1.00133.02
ATOM	1730	O	MET	330	24.615	29.924	84.265	1.00133.02
ATOM	1731	N	PHE	331	23.036	31.109	85.354	1.00 83.63
ATOM	1732	CA	PHE	331	22.607	30.029	86.201	1.00 83.63
ATOM	1733	CB	PHE	331	21.599	30.466	87.280	1.00 83.63
ATOM	1734	CG	PHE	331	22.375	31.106	88.383	1.00 83.63
ATOM	1735	CD1	PHE	331	22.824	32.400	88.281	1.00 83.63
ATOM	1736	CD2	PHE	331	22.650	30.399	89.530	1.00 83.63
ATOM	1737	CE1	PHE	331	23.538	32.971	89.311	1.00 83.63
ATOM	1738	CE2	PHE	331	23.366	30.972	90.557	1.00 83.63
ATOM	1739	CZ	PHE	331	23.812	32.262	90.451	1.00 83.63
ATOM	1740	C	PHE	331	21.992	28.937	85.379	1.00 83.63
ATOM	1741	O	PHE	331	22.178	27.760	85.688	1.00 83.63
ATOM	1742	N	ILE	332	21.228	29.279	84.319	1.00106.83
ATOM	1743	CA	ILE	332	20.640	28.222	83.545	1.00106.83
ATOM	1744	CB	ILE	332	19.753	28.643	82.400	1.00106.83
ATOM	1745	CG2	ILE	332	18.631	29.519	82.984	1.00106.83
ATOM	1746	CG1	ILE	332	20.539	29.315	81.268	1.00106.83
ATOM	1747	CD1	ILE	332	19.748	29.434	79.964	1.00106.83
ATOM	1748	C	ILE	332	21.772	27.428	82.972	1.00106.83
ATOM	1749	O	ILE	332	21.715	26.202	82.906	1.00106.83
ATOM	1750	N	SER	333	22.837	28.125	82.537	1.00 51.79
ATOM	1751	CA	SER	333	24.000	27.510	81.960	1.00 51.79
ATOM	1752	CB	SER	333	25.082	28.555	81.640	1.00 51.79
ATOM	1753	OG	SER	333	24.618	29.446	80.638	1.00 51.79
ATOM	1754	C	SER	333	24.613	26.548	82.947	1.00 51.79
ATOM	1755	O	SER	333	24.893	25.402	82.597	1.00 51.79
ATOM	1756	N	LEU	334	24.843	26.981	84.206	1.00121.38
ATOM	1757	CA	LEU	334	25.440	26.123	85.202	1.00121.38
ATOM	1758	CB	LEU	334	25.762	26.813	86.544	1.00121.38
ATOM	1759	CG	LEU	334	27.176	27.413	86.586	1.00121.38
ATOM	1760	CD2	LEU	334	27.429	28.161	87.905	1.00121.38
ATOM	1761	CD1	LEU	334	27.448	28.271	85.352	1.00121.38
ATOM	1762	C	LEU	334	24.542	24.973	85.501	1.00121.38
ATOM	1763	O	LEU	334	25.001	23.850	85.696	1.00121.38
ATOM	1764	N	PHE	335	23.230	25.226	85.556	1.00159.54
ATOM	1765	CA	PHE	335	22.292	24.196	85.851	1.00159.54
ATOM	1766	CB	PHE	335	20.865	24.767	85.906	1.00159.54
ATOM	1767	CG	PHE	335	19.899	23.684	86.217	1.00159.54
ATOM	1768	CD1	PHE	335	19.906	23.083	87.455	1.00159.54
ATOM	1769	CD2	PHE	335	18.970	23.298	85.280	1.00159.54
ATOM	1770	CE1	PHE	335	19.005	22.091	87.753	1.00159.54
ATOM	1771	CE2	PHE	335	18.069	22.306	85.573	1.00159.54
ATOM	1772	CZ	PHE	335	18.085	21.704	86.810	1.00159.54
ATOM	1773	C	PHE	335	22.388	23.163	84.775	1.00159.54
ATOM	1774	O	PHE	335	22.380	21.967	85.054	1.00159.54
ATOM	1775	N	MET	336	22.458	23.588	83.503	1.00155.16
ATOM	1776	CA	MET	336	22.560	22.615	82.458	1.00155.16
ATOM	1777	CB	MET	336	22.361	23.188	81.042	1.00155.16

ATOM	1778	CG	MET	336	23.323	24.301	80.633	1.00155.16
ATOM	1779	SD	MET	336	23.119	24.827	78.905	1.00155.16
ATOM	1780	CE	MET	336	24.318	23.631	78.251	1.00155.16
ATOM	1781	C	MET	336	23.876	21.912	82.535	1.00155.16
ATOM	1782	O	MET	336	23.932	20.692	82.421	1.00155.16
ATOM	1783	N	ILE	337	24.979	22.643	82.775	1.00107.96
ATOM	1784	CA	ILE	337	26.257	21.998	82.747	1.00107.96
ATOM	1785	CB	ILE	337	27.408	22.968	82.889	1.00107.96
ATOM	1786	CG2	ILE	337	27.325	23.676	84.251	1.00107.96
ATOM	1787	CG1	ILE	337	28.745	22.255	82.635	1.00107.96
ATOM	1788	CD1	ILE	337	29.919	23.221	82.483	1.00107.96
ATOM	1789	C	ILE	337	26.349	20.969	83.830	1.00107.96
ATOM	1790	O	ILE	337	26.711	19.823	83.563	1.00107.96
ATOM	1791	N	LEU	338	26.009	21.320	85.084	1.00143.54
ATOM	1792	CA	LEU	338	26.178	20.325	86.096	1.00143.54
ATOM	1793	CB	LEU	338	26.128	20.815	87.546	1.00143.54
ATOM	1794	CG	LEU	338	24.723	20.956	88.125	1.00143.54
ATOM	1795	CD2	LEU	338	23.877	21.963	87.343	1.00143.54
ATOM	1796	CD1	LEU	338	24.834	21.309	89.605	1.00143.54
ATOM	1797	C	LEU	338	25.176	19.233	85.930	1.00143.54
ATOM	1798	O	LEU	338	25.494	18.064	86.118	1.00143.54
ATOM	1799	N	CYS	339	23.931	19.564	85.556	1.00 53.20
ATOM	1800	CA	CYS	339	22.950	18.526	85.471	1.00 53.20
ATOM	1801	CB	CYS	339	21.552	19.054	85.129	1.00 53.20
ATOM	1802	SG	CYS	339	20.905	20.013	86.534	1.00 53.20
ATOM	1803	C	CYS	339	23.383	17.513	84.458	1.00 53.20
ATOM	1804	O	CYS	339	23.210	16.313	84.665	1.00 53.20
ATOM	1805	N	THR	340	23.978	17.961	83.338	1.00 59.69
ATOM	1806	CA	THR	340	24.410	17.037	82.331	1.00 59.69
ATOM	1807	CB	THR	340	24.867	17.743	81.102	1.00 59.69
ATOM	1808	OG1	THR	340	26.007	18.545	81.373	1.00 59.69
ATOM	1809	CG2	THR	340	23.682	18.627	80.673	1.00 59.69
ATOM	1810	C	THR	340	25.503	16.173	82.890	1.00 59.69
ATOM	1811	O	THR	340	25.566	14.979	82.607	1.00 59.69
ATOM	1812	N	ARG	341	26.400	16.767	83.697	1.00166.50
ATOM	1813	CA	ARG	341	27.485	16.067	84.324	1.00166.50
ATOM	1814	CB	ARG	341	28.540	16.994	84.956	1.00166.50
ATOM	1815	CG	ARG	341	29.402	17.720	83.917	1.00166.50
ATOM	1816	CD	ARG	341	30.426	16.817	83.216	1.00166.50
ATOM	1817	NE	ARG	341	29.666	15.747	82.509	1.00166.50
ATOM	1818	CZ	ARG	341	30.255	14.997	81.531	1.00166.50
ATOM	1819	NH1	ARG	341	31.532	15.268	81.142	1.00166.50
ATOM	1820	NH2	ARG	341	29.559	13.977	80.950	1.00166.50
ATOM	1821	C	ARG	341	26.969	15.144	85.384	1.00166.50
ATOM	1822	O	ARG	341	27.625	14.155	85.703	1.00166.50
ATOM	1823	N	THR	342	25.773	15.453	85.929	1.00243.88
ATOM	1824	CA	THR	342	25.109	14.842	87.056	1.00243.88
ATOM	1825	CB	THR	342	25.115	13.329	87.094	1.00243.88
ATOM	1826	OG1	THR	342	26.378	12.820	87.496	1.00243.88
ATOM	1827	CG2	THR	342	24.757	12.802	85.693	1.00243.88
ATOM	1828	C	THR	342	25.625	15.308	88.408	1.00243.88
ATOM	1829	O	THR	342	25.437	14.562	89.369	1.00243.88
ATOM	1830	N	PRO	343	26.237	16.465	88.607	1.00235.84
ATOM	1831	CA	PRO	343	26.455	16.863	89.969	1.00235.84
ATOM	1832	CD	PRO	343	27.394	16.878	87.814	1.00235.84
ATOM	1833	CB	PRO	343	27.440	18.025	89.938	1.00235.84
ATOM	1834	CG	PRO	343	28.320	17.688	88.732	1.00235.84
ATOM	1835	C	PRO	343	25.199	17.159	90.732	1.00235.84
ATOM	1836	O	PRO	343	25.343	17.430	91.916	1.00235.84
ATOM	1837	N	PRO	344	24.013	17.210	90.200	1.00146.86
ATOM	1838	CA	PRO	344	22.908	17.373	91.105	1.00146.86
ATOM	1839	CD	PRO	344	23.778	17.891	88.936	1.00146.86
ATOM	1840	CB	PRO	344	21.731	17.831	90.252	1.00146.86
ATOM	1841	CG	PRO	344	22.405	18.572	89.085	1.00146.86
ATOM	1842	C	PRO	344	22.725	16.036	91.726	1.00146.86
ATOM	1843	O	PRO	344	23.180	15.072	91.117	1.00146.86

ATOM	1844	N	LYS	345	22.109	15.944	92.923	1.00269.51
ATOM	1845	CA	LYS	345	21.937	14.657	93.535	1.00269.51
ATOM	1846	CB	LYS	345	22.991	14.317	94.601	1.00269.51
ATOM	1847	CG	LYS	345	24.410	14.175	94.054	1.00269.51
ATOM	1848	CD	LYS	345	24.559	13.061	93.019	1.00269.51
ATOM	1849	CE	LYS	345	25.977	12.940	92.455	1.00269.51
ATOM	1850	NZ	LYS	345	26.850	12.229	93.416	1.00269.51
ATOM	1851	C	LYS	345	20.637	14.655	94.265	1.00269.51
ATOM	1852	O	LYS	345	19.963	15.678	94.376	1.00269.51
ATOM	1853	N	SER	346	20.247	13.468	94.770	1.00 69.56
ATOM	1854	CA	SER	346	19.058	13.362	95.555	1.00 69.56
ATOM	1855	CB	SER	346	18.802	11.932	96.066	1.00 69.56
ATOM	1856	OG	SER	346	19.821	11.548	96.979	1.00 69.56
ATOM	1857	C	SER	346	19.293	14.225	96.748	1.00 69.56
ATOM	1858	O	SER	346	18.432	15.003	97.153	1.00 69.56
ATOM	1859	N	PHE	347	20.502	14.110	97.330	1.00222.83
ATOM	1860	CA	PHE	347	20.861	14.913	98.458	1.00222.83
ATOM	1861	CB	PHE	347	21.482	14.125	99.626	1.00222.83
ATOM	1862	CG	PHE	347	20.372	13.414	100.316	1.00222.83
ATOM	1863	CD1	PHE	347	19.858	12.247	99.804	1.00222.83
ATOM	1864	CD2	PHE	347	19.843	13.923	101.481	1.00222.83
ATOM	1865	CE1	PHE	347	18.831	11.598	100.447	1.00222.83
ATOM	1866	CE2	PHE	347	18.816	13.278	102.129	1.00222.83
ATOM	1867	CZ	PHE	347	18.308	12.113	101.609	1.00222.83
ATOM	1868	C	PHE	347	21.879	15.884	97.977	1.00222.83
ATOM	1869	O	PHE	347	22.550	15.648	96.974	1.00222.83
ATOM	1870	N	LYS	348	21.990	17.027	98.681	1.00288.70
ATOM	1871	CA	LYS	348	22.925	18.038	98.299	1.00288.70
ATOM	1872	CB	LYS	348	24.321	17.471	97.993	1.00288.70
ATOM	1873	CG	LYS	348	24.934	16.735	99.186	1.00288.70
ATOM	1874	CD	LYS	348	26.080	15.801	98.798	1.00288.70
ATOM	1875	CE	LYS	348	25.601	14.449	98.265	1.00288.70
ATOM	1876	NZ	LYS	348	26.768	13.593	97.958	1.00288.70
ATOM	1877	C	LYS	348	22.379	18.685	97.068	1.00288.70
ATOM	1878	O	LYS	348	21.881	18.011	96.168	1.00288.70
ATOM	1879	N	SER	349	22.438	20.031	97.016	1.00159.92
ATOM	1880	CA	SER	349	21.932	20.754	95.887	1.00159.92
ATOM	1881	CB	SER	349	21.494	22.193	96.215	1.00159.92
ATOM	1882	OG	SER	349	20.391	22.176	97.112	1.00159.92
ATOM	1883	C	SER	349	23.021	20.837	94.878	1.00159.92
ATOM	1884	O	SER	349	24.086	20.248	95.051	1.00159.92
ATOM	1885	N	LEU	350	22.767	21.569	93.776	1.00150.01
ATOM	1886	CA	LEU	350	23.746	21.711	92.751	1.00150.01
ATOM	1887	CB	LEU	350	23.317	22.709	91.670	1.00150.01
ATOM	1888	CG	LEU	350	22.158	22.234	90.778	1.00150.01
ATOM	1889	CD2	LEU	350	21.987	23.148	89.553	1.00150.01
ATOM	1890	CD1	LEU	350	20.866	22.057	91.587	1.00150.01
ATOM	1891	C	LEU	350	24.986	22.232	93.392	1.00150.01
ATOM	1892	O	LEU	350	24.993	23.291	94.020	1.00150.01
ATOM	1893	N	LYS	351	26.070	21.445	93.267	1.00285.93
ATOM	1894	CA	LYS	351	27.330	21.808	93.827	1.00285.93
ATOM	1895	CB	LYS	351	27.583	21.249	95.236	1.00285.93
ATOM	1896	CG	LYS	351	26.595	21.702	96.300	1.00285.93
ATOM	1897	CD	LYS	351	26.817	21.034	97.659	1.00285.93
ATOM	1898	CE	LYS	351	28.030	21.589	98.414	1.00285.93
ATOM	1899	NZ	LYS	351	28.195	20.882	99.704	1.00285.93
ATOM	1900	C	LYS	351	28.364	21.123	93.007	1.00285.93
ATOM	1901	O	LYS	351	28.060	20.255	92.193	1.00285.93
ATOM	1902	N	LYS	352	29.625	21.540	93.192	1.00262.02
ATOM	1903	CA	LYS	352	30.745	20.865	92.618	1.00262.02
ATOM	1904	CB	LYS	352	31.952	21.787	92.381	1.00262.02
ATOM	1905	CG	LYS	352	31.819	22.672	91.138	1.00262.02
ATOM	1906	CD	LYS	352	30.600	23.594	91.162	1.00262.02
ATOM	1907	CE	LYS	352	29.518	23.209	90.146	1.00262.02
ATOM	1908	NZ	LYS	352	29.188	21.769	90.259	1.00262.02
ATOM	1909	C	LYS	352	31.118	19.856	93.656	1.00262.02

ATOM	1910	O	LYS	352	30.529	19.818	94.732	1.00262.02
ATOM	1911	N	VAL	353	32.064	18.956	93.357	1.00 96.29
ATOM	1912	CA	VAL	353	32.401	18.034	94.396	1.00 96.29
ATOM	1913	CB	VAL	353	33.454	17.048	93.992	1.00 96.29
ATOM	1914	CG1	VAL	353	33.825	16.202	95.221	1.00 96.29
ATOM	1915	CG2	VAL	353	32.929	16.222	92.803	1.00 96.29
ATOM	1916	C	VAL	353	32.962	18.832	95.531	1.00 96.29
ATOM	1917	O	VAL	353	32.568	18.665	96.685	1.00 96.29
ATOM	1918	N	TYR	354	33.900	19.743	95.213	1.00110.82
ATOM	1919	CA	TYR	354	34.573	20.510	96.218	1.00110.82
ATOM	1920	CB	TYR	354	35.752	21.329	95.661	1.00110.82
ATOM	1921	CG	TYR	354	36.565	21.799	96.822	1.00110.82
ATOM	1922	CD1	TYR	354	37.557	20.991	97.328	1.00110.82
ATOM	1923	CD2	TYR	354	36.350	23.026	97.405	1.00110.82
ATOM	1924	CE1	TYR	354	38.322	21.393	98.396	1.00110.82
ATOM	1925	CE2	TYR	354	37.114	23.435	98.475	1.00110.82
ATOM	1926	CZ	TYR	354	38.103	22.620	98.972	1.00110.82
ATOM	1927	OH	TYR	354	38.887	23.040	100.067	1.00110.82
ATOM	1928	C	TYR	354	33.630	21.476	96.875	1.00110.82
ATOM	1929	O	TYR	354	33.613	21.591	98.099	1.00110.82
ATOM	1930	N	THR	355	32.796	22.186	96.086	1.00255.20
ATOM	1931	CA	THR	355	31.997	23.218	96.692	1.00255.20
ATOM	1932	CB	THR	355	32.495	24.598	96.375	1.00255.20
ATOM	1933	OG1	THR	355	32.426	24.834	94.975	1.00255.20
ATOM	1934	CG2	THR	355	33.950	24.725	96.861	1.00255.20
ATOM	1935	C	THR	355	30.593	23.148	96.186	1.00255.20
ATOM	1936	O	THR	355	30.144	22.125	95.686	1.00255.20
ATOM	1937	N	PHE	356	29.847	24.257	96.373	1.00322.17
ATOM	1938	CA	PHE	356	28.493	24.408	95.916	1.00322.17
ATOM	1939	CB	PHE	356	27.639	25.183	96.950	1.00322.17
ATOM	1940	CG	PHE	356	26.183	25.190	96.604	1.00322.17
ATOM	1941	CD1	PHE	356	25.653	26.176	95.805	1.00322.17
ATOM	1942	CD2	PHE	356	25.329	24.227	97.092	1.00322.17
ATOM	1943	CE1	PHE	356	24.315	26.192	95.485	1.00322.17
ATOM	1944	CE2	PHE	356	23.992	24.232	96.779	1.00322.17
ATOM	1945	CZ	PHE	356	23.478	25.217	95.971	1.00322.17
ATOM	1946	C	PHE	356	28.646	25.273	94.705	1.00322.17
ATOM	1947	O	PHE	356	29.539	26.119	94.691	1.00322.17
ATOM	1948	N	PHE	357	27.836	25.084	93.637	1.00120.88
ATOM	1949	CA	PHE	357	28.089	25.979	92.549	1.00120.88
ATOM	1950	CB	PHE	357	27.319	25.680	91.245	1.00120.88
ATOM	1951	CG	PHE	357	25.892	26.079	91.379	1.00120.88
ATOM	1952	CD1	PHE	357	25.525	27.364	91.063	1.00120.88
ATOM	1953	CD2	PHE	357	24.931	25.194	91.801	1.00120.88
ATOM	1954	CE1	PHE	357	24.219	27.770	91.167	1.00120.88
ATOM	1955	CE2	PHE	357	23.623	25.607	91.904	1.00120.88
ATOM	1956	CZ	PHE	357	23.257	26.891	91.590	1.00120.88
ATOM	1957	C	PHE	357	27.698	27.319	93.070	1.00120.88
ATOM	1958	O	PHE	357	26.608	27.501	93.610	1.00120.88
ATOM	1959	N	LYS	358	28.604	28.300	92.942	1.00147.15
ATOM	1960	CA	LYS	358	28.329	29.562	93.552	1.00147.15
ATOM	1961	CB	LYS	358	29.297	29.904	94.692	1.00147.15
ATOM	1962	CG	LYS	358	30.771	29.744	94.321	1.00147.15
ATOM	1963	CD	LYS	358	31.733	30.473	95.261	1.00147.15
ATOM	1964	CE	LYS	358	31.409	30.288	96.743	1.00147.15
ATOM	1965	NZ	LYS	358	30.264	31.151	97.126	1.00147.15
ATOM	1966	C	LYS	358	28.429	30.643	92.538	1.00147.15
ATOM	1967	O	LYS	358	28.609	30.394	91.347	1.00147.15
ATOM	1968	N	PHE	359	28.283	31.889	93.022	1.00116.80
ATOM	1969	CA	PHE	359	28.319	33.059	92.206	1.00116.80
ATOM	1970	CB	PHE	359	27.859	34.340	92.937	1.00116.80
ATOM	1971	CG	PHE	359	28.713	34.619	94.120	1.00116.80
ATOM	1972	CD1	PHE	359	28.456	34.001	95.325	1.00116.80
ATOM	1973	CD2	PHE	359	29.767	35.498	94.036	1.00116.80
ATOM	1974	CE1	PHE	359	29.237	34.255	96.427	1.00116.80
ATOM	1975	CE2	PHE	359	30.549	35.757	95.135	1.00116.80

ATOM	1976	CZ	PHE	359	30.285	35.136	96.333	1.00116.80
ATOM	1977	C	PHE	359	29.687	33.211	91.623	1.00116.80
ATOM	1978	O	PHE	359	29.829	33.701	90.505	1.00116.80
ATOM	1979	N	LEU	360	30.742	32.806	92.360	1.00 80.96
ATOM	1980	CA	LEU	360	32.057	32.919	91.795	1.00 80.96
ATOM	1981	CB	LEU	360	33.203	32.471	92.725	1.00 80.96
ATOM	1982	CG	LEU	360	33.432	33.416	93.923	1.00 80.96
ATOM	1983	CD2	LEU	360	34.798	33.177	94.586	1.00 80.96
ATOM	1984	CD1	LEU	360	32.260	33.365	94.915	1.00 80.96
ATOM	1985	C	LEU	360	32.093	32.064	90.567	1.00 80.96
ATOM	1986	O	LEU	360	32.682	32.447	89.557	1.00 80.96
ATOM	1987	N	ALA	361	31.450	30.882	90.622	1.00 33.90
ATOM	1988	CA	ALA	361	31.404	30.015	89.480	1.00 33.90
ATOM	1989	CB	ALA	361	30.636	28.711	89.746	1.00 33.90
ATOM	1990	C	ALA	361	30.683	30.761	88.399	1.00 33.90
ATOM	1991	O	ALA	361	31.024	30.680	87.220	1.00 33.90
ATOM	1992	N	ASP	362	29.652	31.531	88.776	1.00 92.51
ATOM	1993	CA	ASP	362	28.901	32.266	87.801	1.00 92.51
ATOM	1994	CB	ASP	362	27.776	33.095	88.461	1.00 92.51
ATOM	1995	CG	ASP	362	26.929	33.822	87.417	1.00 92.51
ATOM	1996	OD1	ASP	362	27.501	34.539	86.554	1.00 92.51
ATOM	1997	OD2	ASP	362	25.681	33.659	87.473	1.00 92.51
ATOM	1998	C	ASP	362	29.829	33.214	87.101	1.00 92.51
ATOM	1999	O	ASP	362	29.778	33.357	85.880	1.00 92.51
ATOM	2000	N	LYS	363	30.713	33.889	87.858	1.00102.78
ATOM	2001	CA	LYS	363	31.580	34.866	87.261	1.00102.78
ATOM	2002	CB	LYS	363	32.441	35.585	88.315	1.00102.78
ATOM	2003	CG	LYS	363	33.389	36.645	87.750	1.00102.78
ATOM	2004	CD	LYS	363	33.968	37.566	88.828	1.00102.78
ATOM	2005	CE	LYS	363	35.188	38.365	88.370	1.00102.78
ATOM	2006	NZ	LYS	363	36.386	37.488	88.348	1.00102.78
ATOM	2007	C	LYS	363	32.496	34.220	86.264	1.00102.78
ATOM	2008	O	LYS	363	32.609	34.680	85.129	1.00102.78
ATOM	2009	N	LYS	364	33.170	33.120	86.648	1.00 86.80
ATOM	2010	CA	LYS	364	34.086	32.497	85.736	1.00 86.80
ATOM	2011	CB	LYS	364	35.057	31.490	86.379	1.00 86.80
ATOM	2012	CG	LYS	364	36.209	32.158	87.136	1.00 86.80
ATOM	2013	CD	LYS	364	37.021	31.212	88.023	1.00 86.80
ATOM	2014	CE	LYS	364	36.440	31.043	89.428	1.00 86.80
ATOM	2015	NZ	LYS	364	37.385	30.291	90.284	1.00 86.80
ATOM	2016	C	LYS	364	33.344	31.863	84.602	1.00 86.80
ATOM	2017	O	LYS	364	33.873	31.749	83.498	1.00 86.80
ATOM	2018	N	MET	365	32.092	31.429	84.831	1.00 53.49
ATOM	2019	CA	MET	365	31.359	30.755	83.796	1.00 53.49
ATOM	2020	CB	MET	365	29.982	30.264	84.255	1.00 53.49
ATOM	2021	CG	MET	365	29.226	29.461	83.196	1.00 53.49
ATOM	2022	SD	MET	365	29.905	27.805	82.885	1.00 53.49
ATOM	2023	CE	MET	365	28.617	27.319	81.701	1.00 53.49
ATOM	2024	C	MET	365	31.170	31.664	82.625	1.00 53.49
ATOM	2025	O	MET	365	31.208	31.220	81.478	1.00 53.49
ATOM	2026	N	THR	366	30.951	32.966	82.866	1.00 70.35
ATOM	2027	CA	THR	366	30.705	33.792	81.730	1.00 70.35
ATOM	2028	CB	THR	366	30.255	35.162	82.075	1.00 70.35
ATOM	2029	OG1	THR	366	29.230	35.112	83.058	1.00 70.35
ATOM	2030	CG2	THR	366	29.616	35.667	80.778	1.00 70.35
ATOM	2031	C	THR	366	31.948	33.865	80.887	1.00 70.35
ATOM	2032	O	THR	366	31.868	33.895	79.660	1.00 70.35
ATOM	2033	N	LEU	367	33.136	33.919	81.526	1.00 81.70
ATOM	2034	CA	LEU	367	34.382	33.971	80.809	1.00 81.70
ATOM	2035	CB	LEU	367	35.609	34.150	81.721	1.00 81.70
ATOM	2036	CG	LEU	367	35.688	35.525	82.413	1.00 81.70
ATOM	2037	CD2	LEU	367	37.070	35.740	83.050	1.00 81.70
ATOM	2038	CD1	LEU	367	34.531	35.733	83.400	1.00 81.70
ATOM	2039	C	LEU	367	34.564	32.683	80.071	1.00 81.70
ATOM	2040	O	LEU	367	35.063	32.663	78.947	1.00 81.70
ATOM	2041	N	PHE	368	34.163	31.566	80.708	1.00 59.75

ATOM	2042	CA	PHE	368	34.302	30.249	80.153	1.00	59.75
ATOM	2043	CB	PHE	368	33.778	29.185	81.136	1.00	59.75
ATOM	2044	CG	PHE	368	33.868	27.826	80.529	1.00	59.75
ATOM	2045	CD1	PHE	368	35.075	27.174	80.426	1.00	59.75
ATOM	2046	CD2	PHE	368	32.731	27.191	80.091	1.00	59.75
ATOM	2047	CE1	PHE	368	35.143	25.915	79.873	1.00	59.75
ATOM	2048	CE2	PHE	368	32.792	25.932	79.538	1.00	59.75
ATOM	2049	CZ	PHE	368	34.003	25.293	79.427	1.00	59.75
ATOM	2050	C	PHE	368	33.512	30.169	78.886	1.00	59.75
ATOM	2051	O	PHE	368	34.011	29.728	77.853	1.00	59.75
ATOM	2052	N	LYS	369	32.250	30.623	78.918	1.00	110.95
ATOM	2053	CA	LYS	369	31.446	30.530	77.736	1.00	110.95
ATOM	2054	CB	LYS	369	30.015	31.029	77.952	1.00	110.95
ATOM	2055	CG	LYS	369	29.190	30.880	76.683	1.00	110.95
ATOM	2056	CD	LYS	369	27.688	30.943	76.907	1.00	110.95
ATOM	2057	CE	LYS	369	26.937	30.514	75.656	1.00	110.95
ATOM	2058	NZ	LYS	369	27.482	29.223	75.183	1.00	110.95
ATOM	2059	C	LYS	369	32.063	31.367	76.659	1.00	110.95
ATOM	2060	O	LYS	369	32.098	30.975	75.494	1.00	110.95
ATOM	2061	N	SER	370	32.579	32.549	77.028	1.00	75.96
ATOM	2062	CA	SER	370	33.162	33.448	76.078	1.00	75.96
ATOM	2063	CB	SER	370	33.710	34.714	76.757	1.00	75.96
ATOM	2064	OG	SER	370	34.387	35.523	75.810	1.00	75.96
ATOM	2065	C	SER	370	34.315	32.775	75.399	1.00	75.96
ATOM	2066	O	SER	370	34.474	32.884	74.184	1.00	75.96
ATOM	2067	N	ILE	371	35.154	32.052	76.163	1.00	124.77
ATOM	2068	CA	ILE	371	36.307	31.439	75.569	1.00	124.77
ATOM	2069	CB	ILE	371	37.271	30.824	76.546	1.00	124.77
ATOM	2070	CG2	ILE	371	36.641	29.548	77.119	1.00	124.77
ATOM	2071	CG1	ILE	371	38.620	30.560	75.853	1.00	124.77
ATOM	2072	CD1	ILE	371	39.348	31.834	75.428	1.00	124.77
ATOM	2073	C	ILE	371	35.882	30.387	74.597	1.00	124.77
ATOM	2074	O	ILE	371	36.477	30.250	73.530	1.00	124.77
ATOM	2075	N	LEU	372	34.838	29.605	74.927	1.00	105.73
ATOM	2076	CA	LEU	372	34.451	28.565	74.019	1.00	105.73
ATOM	2077	CB	LEU	372	33.292	27.682	74.510	1.00	105.73
ATOM	2078	CG	LEU	372	33.737	26.614	75.522	1.00	105.73
ATOM	2079	CD2	LEU	372	32.585	25.650	75.845	1.00	105.73
ATOM	2080	CD1	LEU	372	34.372	27.235	76.772	1.00	105.73
ATOM	2081	C	LEU	372	34.060	29.165	72.714	1.00	105.73
ATOM	2082	O	LEU	372	34.364	28.606	71.662	1.00	105.73
ATOM	2083	N	PHE	373	33.365	30.314	72.732	1.00	64.70
ATOM	2084	CA	PHE	373	32.945	30.855	71.478	1.00	64.70
ATOM	2085	CB	PHE	373	31.996	32.050	71.593	1.00	64.70
ATOM	2086	CG	PHE	373	31.471	32.113	70.211	1.00	64.70
ATOM	2087	CD1	PHE	373	30.661	31.089	69.784	1.00	64.70
ATOM	2088	CD2	PHE	373	31.779	33.147	69.361	1.00	64.70
ATOM	2089	CE1	PHE	373	30.154	31.086	68.513	1.00	64.70
ATOM	2090	CE2	PHE	373	31.269	33.146	68.086	1.00	64.70
ATOM	2091	CZ	PHE	373	30.458	32.118	67.664	1.00	64.70
ATOM	2092	C	PHE	373	34.131	31.280	70.664	1.00	64.70
ATOM	2093	O	PHE	373	34.206	30.989	69.472	1.00	64.70
ATOM	2094	N	ASN	374	35.105	31.971	71.286	1.00	35.72
ATOM	2095	CA	ASN	374	36.247	32.451	70.559	1.00	35.72
ATOM	2096	CB	ASN	374	37.207	33.269	71.437	1.00	35.72
ATOM	2097	CG	ASN	374	36.483	34.537	71.865	1.00	35.72
ATOM	2098	OD1	ASN	374	35.692	35.105	71.114	1.00	35.72
ATOM	2099	ND2	ASN	374	36.758	34.995	73.115	1.00	35.72
ATOM	2100	C	ASN	374	37.011	31.277	70.026	1.00	35.72
ATOM	2101	O	ASN	374	37.540	31.315	68.917	1.00	35.72
ATOM	2102	N	LEU	375	37.099	30.205	70.833	1.00	138.95
ATOM	2103	CA	LEU	375	37.815	29.003	70.512	1.00	138.95
ATOM	2104	CB	LEU	375	37.964	28.066	71.731	1.00	138.95
ATOM	2105	CG	LEU	375	38.995	26.926	71.570	1.00	138.95
ATOM	2106	CD2	LEU	375	40.379	27.498	71.223	1.00	138.95
ATOM	2107	CD1	LEU	375	38.548	25.833	70.589	1.00	138.95

ATOM	2108	C	LEU	375	37.093	28.291	69.406	1.00138.95
ATOM	2109	O	LEU	375	37.711	27.552	68.641	1.00138.95
ATOM	2110	N	HIS	376	35.766	28.517	69.292	1.00123.01
ATOM	2111	CA	HIS	376	34.901	27.828	68.370	1.00123.01
ATOM	2112	ND1	HIS	376	36.992	27.064	65.722	1.00123.01
ATOM	2113	CG	HIS	376	36.407	28.177	66.282	1.00123.01
ATOM	2114	CB	HIS	376	35.031	28.206	66.871	1.00123.01
ATOM	2115	NE2	HIS	376	38.477	28.713	65.561	1.00123.01
ATOM	2116	CD2	HIS	376	37.327	29.175	66.176	1.00123.01
ATOM	2117	CE1	HIS	376	38.228	27.440	65.307	1.00123.01
ATOM	2118	C	HIS	376	35.014	26.360	68.605	1.00123.01
ATOM	2119	O	HIS	376	35.402	25.581	67.735	1.00123.01
ATOM	2120	N	ASP	377	34.645	25.976	69.845	1.00 65.93
ATOM	2121	CA	ASP	377	34.668	24.635	70.353	1.00 65.93
ATOM	2122	CB	ASP	377	34.286	24.519	71.842	1.00 65.93
ATOM	2123	CG	ASP	377	35.531	24.786	72.676	1.00 65.93
ATOM	2124	OD1	ASP	377	36.651	24.598	72.132	1.00 65.93
ATOM	2125	OD2	ASP	377	35.380	25.159	73.869	1.00 65.93
ATOM	2126	C	ASP	377	33.737	23.760	69.578	1.00 65.93
ATOM	2127	O	ASP	377	33.945	22.551	69.506	1.00 65.93
ATOM	2128	N	LEU	378	32.671	24.325	68.988	1.00 87.86
ATOM	2129	CA	LEU	378	31.748	23.489	68.277	1.00 87.86
ATOM	2130	CB	LEU	378	30.589	24.271	67.642	1.00 87.86
ATOM	2131	CG	LEU	378	29.593	24.813	68.680	1.00 87.86
ATOM	2132	CD2	LEU	378	30.294	25.697	69.726	1.00 87.86
ATOM	2133	CD1	LEU	378	28.792	23.673	69.319	1.00 87.86
ATOM	2134	C	LEU	378	32.477	22.779	67.182	1.00 87.86
ATOM	2135	O	LEU	378	32.211	21.606	66.929	1.00 87.86
ATOM	2136	N	SER	379	33.403	23.460	66.483	1.00 17.91
ATOM	2137	CA	SER	379	34.122	22.754	65.465	1.00 17.91
ATOM	2138	CB	SER	379	34.647	23.656	64.331	1.00 17.91
ATOM	2139	OG	SER	379	35.608	24.576	64.827	1.00 17.91
ATOM	2140	C	SER	379	35.317	22.106	66.145	1.00 17.91
ATOM	2141	O	SER	379	36.181	22.858	66.669	1.00 17.91
ATOM	2142	OXT	SER	379	35.380	20.848	66.153	1.00 17.91

END

TABLE-3

REMARK	4	TTP-A Computed low-energy docking mode-1						
REMARK		Free Energy of Binding = -11.24 kcal/mol						
ATOM	1	C9	MOL	1	14.331	35.024	76.250	-0.49
ATOM	2	C4	MOL	1	15.175	35.446	77.272	-0.50
ATOM	3	C12	MOL	1	14.648	35.356	74.948	-0.41
ATOM	4	C1	MOL	1	16.340	36.195	77.047	-0.52
ATOM	5	C3	MOL	1	16.661	36.522	75.696	-0.49
ATOM	6	C7	MOL	1	15.793	36.088	74.698	-0.42
ATOM	7	C14	MOL	1	13.069	34.215	76.522	-0.35
ATOM	8	C16	MOL	1	12.147	35.063	77.449	-0.61
ATOM	9	N17	MOL	1	10.746	34.939	77.134	-0.19
ATOM	10	H17	MOL	1	10.090	34.523	77.810	-0.19
ATOM	11	C18	MOL	1	10.294	35.400	75.880	-0.47
ATOM	12	O20	MOL	1	11.112	35.909	75.103	+0.04
ATOM	13	C19	MOL	1	8.875	35.299	75.453	-0.39
ATOM	14	C22	MOL	1	8.475	34.568	74.332	-0.31
ATOM	15	O25	MOL	1	9.402	33.882	73.533	-0.10
ATOM	16	H25	MOL	1	9.655	33.026	73.978	-0.14
ATOM	17	C24	MOL	1	7.129	34.514	73.990	-0.26
ATOM	18	C30	MOL	1	3.884	35.791	75.169	-0.09
ATOM	19	C28	MOL	1	4.833	35.121	74.403	-0.13
ATOM	20	C27	MOL	1	5.623	36.575	76.636	-0.25
ATOM	21	C29	MOL	1	4.281	36.517	76.287	-0.15
ATOM	22	C26	MOL	1	6.177	35.180	74.753	-0.18
ATOM	23	C23	MOL	1	6.572	35.908	75.868	-0.27
ATOM	24	C21	MOL	1	7.916	35.963	76.214	-0.39
ATOM	25	C2	MOL	1	17.063	36.529	78.390	-0.54
ATOM	26	C6	MOL	1	17.552	35.601	79.301	-0.75
ATOM	27	C11	MOL	1	18.194	35.978	80.472	-0.84
ATOM	28	C15	MOL	1	18.364	37.322	80.761	-0.83
ATOM	29	N1	MOL	1	19.005	37.698	81.944	-0.59
ATOM	30	O2	MOL	1	18.437	38.366	82.727	-0.29
ATOM	31	O3	MOL	1	20.246	37.308	82.183	-0.77
ATOM	32	C10	MOL	1	17.889	38.277	79.867	-0.73
ATOM	33	C5	MOL	1	17.251	37.877	78.694	-0.60
ATOM	34	O8	MOL	1	17.778	37.255	75.046	+0.02
ATOM	35	C13	MOL	1	17.743	38.555	74.504	-0.36
END								
REMARK		TTP-A Computed low-energy docking mode-2						
REMARK		Free Energy of Binding = -11.24 kcal/mol						
ATOM	1	C9	MOL	2	14.546	35.957	75.646	-0.41
ATOM	2	C4	MOL	2	15.319	36.210	76.776	-0.43
ATOM	3	C12	MOL	2	14.848	36.618	74.473	-0.33
ATOM	4	C1	MOL	2	16.397	37.106	76.783	-0.49
ATOM	5	C3	MOL	2	16.705	37.776	75.560	-0.43
ATOM	6	C7	MOL	2	15.909	37.503	74.451	-0.35
ATOM	7	C14	MOL	2	13.377	34.979	75.667	-0.40
ATOM	8	C16	MOL	2	12.063	35.802	75.507	-0.40
ATOM	9	N17	MOL	2	10.877	34.985	75.452	-0.12
ATOM	10	H17	MOL	2	10.840	34.151	74.849	+0.28
ATOM	11	C18	MOL	2	9.769	35.352	76.244	-0.52
ATOM	12	O20	MOL	2	9.861	36.351	76.969	-0.12
ATOM	13	C19	MOL	2	8.495	34.588	76.243	-0.49
ATOM	14	C22	MOL	2	7.581	34.648	75.187	-0.31
ATOM	15	O25	MOL	2	7.816	35.443	74.057	+0.13
ATOM	16	H25	MOL	2	8.798	35.512	73.896	+0.11
ATOM	17	C24	MOL	2	6.408	33.905	75.251	-0.29
ATOM	18	C30	MOL	2	4.690	31.567	77.516	-0.33
ATOM	19	C28	MOL	2	4.959	32.366	76.409	-0.31
ATOM	20	C27	MOL	2	6.774	32.243	78.510	-0.59
ATOM	21	C29	MOL	2	5.599	31.506	78.566	-0.47
ATOM	22	C26	MOL	2	6.135	33.104	76.354	-0.36
ATOM	23	C23	MOL	2	7.042	33.044	77.405	-0.54
ATOM	24	C21	MOL	2	8.216	33.783	77.344	-0.53

ATOM	25	C2	MOL	2	17.054	37.186	78.197	-0.46
ATOM	26	C6	MOL	2	17.338	36.106	79.022	-0.65
ATOM	27	C11	MOL	2	17.934	36.258	80.266	-0.82
ATOM	28	C15	MOL	2	18.266	37.524	80.719	-0.82
ATOM	29	N1	MOL	2	18.860	37.674	81.974	-0.55
ATOM	30	O2	MOL	2	18.306	38.286	82.812	-0.23
ATOM	31	O3	MOL	2	20.042	37.134	82.222	-0.76
ATOM	32	C10	MOL	2	17.999	38.628	79.915	-0.61
ATOM	33	C5	MOL	2	17.404	38.452	78.666	-0.61
ATOM	34	O8	MOL	2	17.746	38.753	75.149	+0.00
ATOM	35	C13	MOL	2	17.705	40.154	75.297	-0.29

END

REMARK TTP-A Computed low-energy docking mode-3

REMARK Free Energy of Binding = -11.24 kcal/mol

ATOM	1	C9	MOL	3	17.997	38.677	73.823	-0.35
ATOM	2	C4	MOL	3	17.513	37.647	74.624	-0.35
ATOM	3	C12	MOL	3	18.452	39.831	74.429	-0.29
ATOM	4	C1	MOL	3	17.465	37.720	76.024	-0.42
ATOM	5	C3	MOL	3	17.948	38.915	76.638	-0.44
ATOM	6	C7	MOL	3	18.421	39.927	75.807	-0.39
ATOM	7	C14	MOL	3	18.036	38.573	72.304	-0.34
ATOM	8	C16	MOL	3	16.629	38.966	71.761	-0.19
ATOM	9	N17	MOL	3	15.601	38.008	72.082	-0.28
ATOM	10	H17	MOL	3	15.740	37.005	71.896	-0.22
ATOM	11	C18	MOL	3	14.401	38.475	72.657	-0.15
ATOM	12	O20	MOL	3	14.280	39.687	72.881	+0.17
ATOM	13	C19	MOL	3	13.274	37.571	73.004	-0.17
ATOM	14	C22	MOL	3	12.524	36.896	72.038	-0.16
ATOM	15	O25	MOL	3	12.793	37.037	70.669	+0.18
ATOM	16	H25	MOL	3	13.755	36.838	70.497	+0.10
ATOM	17	C24	MOL	3	11.483	36.064	72.434	-0.22
ATOM	18	C30	MOL	3	9.839	34.901	75.515	-0.38
ATOM	19	C28	MOL	3	10.138	35.063	74.166	-0.24
ATOM	20	C27	MOL	3	11.629	36.404	76.092	-0.38
ATOM	21	C29	MOL	3	10.587	35.572	76.478	-0.54
ATOM	22	C26	MOL	3	11.181	35.897	73.780	-0.26
ATOM	23	C23	MOL	3	11.925	36.568	74.743	-0.30
ATOM	24	C21	MOL	3	12.967	37.399	74.351	-0.25
ATOM	25	C2	MOL	3	16.858	36.418	76.636	-0.54
ATOM	26	C6	MOL	3	17.578	35.307	77.056	-0.61
ATOM	27	C11	MOL	3	16.964	34.188	77.600	-0.64
ATOM	28	C15	MOL	3	15.586	34.159	77.739	-0.69
ATOM	29	N1	MOL	3	14.972	33.028	78.281	-0.52
ATOM	30	O2	MOL	3	14.651	33.025	79.413	-0.21
ATOM	31	O3	MOL	3	14.752	31.962	77.529	-0.27
ATOM	32	C10	MOL	3	14.836	35.257	77.331	-0.54
ATOM	33	C5	MOL	3	15.473	36.374	76.791	-0.43
ATOM	34	O8	MOL	3	18.089	39.372	78.044	-0.15
ATOM	35	C13	MOL	3	17.310	38.979	79.150	-0.69

END

REMARK TTP-A Computed low-energy docking mode-4

REMARK Free Energy of Binding = -11.24 kcal/mol

ATOM	1	C9	MOL	4	10.690	36.976	72.708	-0.14
ATOM	2	C4	MOL	4	9.929	36.252	73.621	-0.21
ATOM	3	C12	MOL	4	10.923	38.314	72.951	-0.11
ATOM	4	C1	MOL	4	9.385	36.815	74.784	-0.25
ATOM	5	C3	MOL	4	9.642	38.198	75.029	-0.27
ATOM	6	C7	MOL	4	10.402	38.893	74.093	-0.18
ATOM	7	C14	MOL	4	11.267	36.340	71.449	-0.17
ATOM	8	C16	MOL	4	12.241	35.206	71.890	-0.28
ATOM	9	N17	MOL	4	12.937	35.491	73.119	-0.17
ATOM	10	H17	MOL	4	12.485	36.039	73.864	+0.10
ATOM	11	C18	MOL	4	14.251	35.003	73.278	-0.27
ATOM	12	O20	MOL	4	14.751	34.334	72.365	-0.29
ATOM	13	C19	MOL	4	15.059	35.261	74.498	-0.42
ATOM	14	C22	MOL	4	16.165	36.114	74.503	-0.41

ATOM	15	O25	MOL	4	16.584	36.781	73.342	-0.21
ATOM	16	H25	MOL	4	15.824	36.835	72.698	-0.17
ATOM	17	C24	MOL	4	16.876	36.310	75.681	-0.50
ATOM	18	C30	MOL	4	16.832	35.223	79.197	-0.76
ATOM	19	C28	MOL	4	17.215	35.870	78.027	-0.58
ATOM	20	C27	MOL	4	15.013	34.174	78.022	-0.74
ATOM	21	C29	MOL	4	15.729	34.375	79.194	-0.69
ATOM	22	C26	MOL	4	16.497	35.667	76.854	-0.55
ATOM	23	C23	MOL	4	15.397	34.818	76.851	-0.55
ATOM	24	C21	MOL	4	14.683	34.621	75.676	-0.45
ATOM	25	C2	MOL	4	8.571	35.757	75.595	-0.37
ATOM	26	C6	MOL	4	7.192	35.599	75.566	-0.28
ATOM	27	C11	MOL	4	6.540	34.626	76.311	-0.35
ATOM	28	C15	MOL	4	7.275	33.771	77.117	-0.52
ATOM	29	N1	MOL	4	6.615	32.797	77.870	-0.34
ATOM	30	O2	MOL	4	6.313	33.026	78.983	-0.12
ATOM	31	O3	MOL	4	6.333	31.619	77.337	-0.05
ATOM	32	C10	MOL	4	8.659	33.901	77.165	-0.44
ATOM	33	C5	MOL	4	9.294	34.882	76.405	-0.52
ATOM	34	O8	MOL	4	9.280	39.141	76.118	-0.03
ATOM	35	C13	MOL	4	8.017	39.717	76.363	-0.25

END

REMARK TTP-A Computed low-energy docking mode-5

REMARK Free Energy of Binding = -11.24 kcal/mol

ATOM	1	C9	MOL	5	13.105	36.487	73.198	-0.23
ATOM	2	C4	MOL	5	11.920	36.000	72.657	-0.23
ATOM	3	C12	MOL	5	13.046	37.547	74.081	-0.23
ATOM	4	C1	MOL	5	10.659	36.532	72.965	-0.18
ATOM	5	C3	MOL	5	10.612	37.621	73.887	-0.18
ATOM	6	C7	MOL	5	11.817	38.087	74.405	-0.18
ATOM	7	C14	MOL	5	14.463	35.893	72.844	-0.13
ATOM	8	C16	MOL	5	14.872	34.918	73.989	-0.37
ATOM	9	N17	MOL	5	15.745	35.515	74.967	-0.28
ATOM	10	H17	MOL	5	16.727	35.724	74.738	-0.00
ATOM	11	C18	MOL	5	15.225	35.808	76.245	-0.45
ATOM	12	O20	MOL	5	14.035	35.558	76.475	-0.04
ATOM	13	C19	MOL	5	16.049	36.404	77.329	-0.46
ATOM	14	C22	MOL	5	16.163	37.784	77.517	-0.33
ATOM	15	O25	MOL	5	15.500	38.696	76.683	-0.02
ATOM	16	H25	MOL	5	14.531	38.465	76.641	+0.09
ATOM	17	C24	MOL	5	16.951	38.273	78.552	-0.62
ATOM	18	C30	MOL	5	19.086	37.030	81.280	-0.78
ATOM	19	C28	MOL	5	18.412	37.904	80.433	-0.77
ATOM	20	C27	MOL	5	18.187	35.158	80.063	-0.78
ATOM	21	C29	MOL	5	18.972	35.656	81.094	-0.67
ATOM	22	C26	MOL	5	17.626	37.405	79.401	-0.59
ATOM	23	C23	MOL	5	17.515	36.032	79.216	-0.67
ATOM	24	C21	MOL	5	16.727	35.539	78.184	-0.65
ATOM	25	C2	MOL	5	9.528	35.786	72.190	-0.19
ATOM	26	C6	MOL	5	9.139	36.037	70.880	-0.13
ATOM	27	C11	MOL	5	8.127	35.322	70.256	-0.06
ATOM	28	C15	MOL	5	7.470	34.317	70.946	-0.22
ATOM	29	N1	MOL	5	6.448	33.603	70.316	-0.41
ATOM	30	O2	MOL	5	5.410	34.120	70.120	+0.13
ATOM	31	O3	MOL	5	6.642	32.348	69.943	-0.23
ATOM	32	C10	MOL	5	7.838	34.037	72.258	-0.34
ATOM	33	C5	MOL	5	8.860	34.764	72.865	-0.31
ATOM	34	O8	MOL	5	9.514	38.430	74.478	+0.14
ATOM	35	C13	MOL	5	8.926	38.269	75.749	-0.34

END

Table-4

REMARK	4	Computed Free energy of binding = -10.68kcal/mol						
REMARK	TTP-B	Computed low-energy docking mode-1						
ATOM	1	C1	TTB	1	16.460	36.607	76.845	-0.00 0.51
ATOM	2	C3	TTB	1	15.068	36.607	76.816	-0.00 0.27
ATOM	3	C4	TTB	1	17.148	35.418	77.039	-0.00 0.61
ATOM	4	C7	TTB	1	14.360	35.417	76.974	-0.00 0.51
ATOM	5	C8	TTB	1	16.447	34.230	77.202	-0.00 0.66
ATOM	6	C12	TTB	1	15.058	34.223	77.169	-0.00 0.63
ATOM	7	C2	TTB	1	17.213	37.852	76.663	-0.00 0.48
ATOM	8	C5	TTB	1	17.535	38.651	77.755	-0.00 0.51
ATOM	9	C9	TTB	1	18.241	39.834	77.565	-0.00 0.51
ATOM	10	C13	TTB	1	18.621	40.220	76.284	-0.00 0.44
ATOM	11	C	TTB	1	19.378	41.498	76.076	-0.00 0.34
ATOM	12	F2	TTB	1	19.510	42.182	77.268	-0.00 0.28
ATOM	13	F3	TTB	1	20.635	41.175	75.610	-0.00 0.35
ATOM	14	F4	TTB	1	18.761	42.258	75.105	-0.00 0.12
ATOM	15	C10	TTB	1	18.301	39.422	75.193	-0.00 0.36
ATOM	16	C6	TTB	1	17.596	38.240	75.383	-0.00 0.40
ATOM	17	C11	TTB	1	12.874	35.461	76.923	-0.00 0.57
ATOM	18	O15	TTB	1	12.223	34.713	77.662	-0.00 0.12
ATOM	19	N14	TTB	1	12.209	36.345	76.056	-0.00 0.26
ATOM	20	C17	TTB	1	10.796	36.441	76.065	-0.00 0.46
ATOM	21	C18	TTB	1	10.270	35.386	75.053	-0.00 0.34
ATOM	22	C20	TTB	1	9.070	34.590	75.558	-0.00 0.42
ATOM	23	C23	TTB	1	7.858	34.704	74.888	-0.00 0.30
ATOM	24	C26	TTB	1	6.751	33.978	75.314	-0.00 0.29
ATOM	25	C28	TTB	1	6.852	33.133	76.413	-0.00 0.37
ATOM	26	C29	TTB	1	5.684	32.375	76.857	-0.00 0.37
ATOM	27	C30	TTB	1	4.745	32.975	77.688	-0.00 0.28
ATOM	28	C32	TTB	1	3.634	32.260	78.113	-0.00 0.21
ATOM	29	C34	TTB	1	3.460	30.940	77.709	-0.00 0.27
ATOM	30	F36	TTB	1	2.387	30.249	78.123	-0.00 0.18
ATOM	31	C33	TTB	1	4.397	30.339	76.879	-0.00 0.43
ATOM	32	C31	TTB	1	5.510	31.056	76.451	-0.00 0.47
ATOM	33	C27	TTB	1	8.062	33.011	77.085	-0.00 0.43
ATOM	34	C24	TTB	1	9.168	33.737	76.656	-0.00 0.47
ATOM	35	C19	TTB	1	10.463	37.836	75.633	-0.00 0.21
ATOM	36	O22	TTB	1	11.083	38.357	74.697	0.00 0.09
ATOM	37	O21	TTB	1	9.471	38.542	76.299	-0.00 0.06
ATOM	38	C25	TTB	1	9.019	39.626	75.493	-0.00 0.28
ATOM	39	O16	TTB	1	14.394	33.003	77.335	-0.00 0.15
ATOM	40	H14	TTB	1	12.755	36.931	75.407	0.00 0.09
ATOM	41	H16	TTB	1	14.333	32.541	76.458	0.00 0.03
END								
REMARK	4	Computed low-energy docking mode-2						
REMARK	TTP-B	Computed Free energy of binding = -9.51kcal/mol						
ATOM	1	C1	TTB	2	11.151	36.020	75.575	-0.00 0.41
ATOM	2	C3	TTB	2	10.922	35.738	74.231	-0.00 0.28
ATOM	3	C4	TTB	2	10.133	36.554	76.352	-0.00 0.50
ATOM	4	C7	TTB	2	9.674	35.983	73.662	-0.00 0.22
ATOM	5	C8	TTB	2	8.888	36.804	75.789	-0.00 0.37
ATOM	6	C12	TTB	2	8.654	36.520	74.449	-0.00 0.20
ATOM	7	C2	TTB	2	12.456	35.751	76.186	-0.00 0.49
ATOM	8	C5	TTB	2	12.595	34.762	77.154	-0.00 0.54
ATOM	9	C9	TTB	2	13.838	34.526	77.732	-0.00 0.65
ATOM	10	C13	TTB	2	14.940	35.280	77.344	-0.00 0.53
ATOM	11	C	TTB	2	16.280	35.031	77.970	-0.00 0.65
ATOM	12	F2	TTB	2	17.004	36.205	78.046	-0.00 0.44
ATOM	13	F3	TTB	2	16.070	34.559	79.248	-0.00 0.54
ATOM	14	F4	TTB	2	16.951	34.050	77.273	-0.00 0.52
ATOM	15	C10	TTB	2	14.803	36.268	76.377	-0.00 0.42
ATOM	16	C6	TTB	2	13.562	36.503	75.799	-0.00 0.37

ATOM	17	C11	TTB	2	9.471	35.654	72.225	-0.00	0.20
ATOM	18	O15	TTB	2	9.001	34.550	71.921	-0.00	0.23
ATOM	19	N14	TTB	2	9.794	36.582	71.220	-0.00	0.12
ATOM	20	C17	TTB	2	9.527	36.296	69.859	-0.00	0.12
ATOM	21	C18	TTB	2	10.801	36.688	69.061	-0.00	0.11
ATOM	22	C20	TTB	2	11.963	35.716	69.239	-0.00	0.17
ATOM	23	C23	TTB	2	12.818	35.881	70.323	-0.00	0.22
ATOM	24	C26	TTB	2	13.876	35.001	70.522	-0.00	0.30
ATOM	25	C28	TTB	2	14.084	33.950	69.636	-0.00	0.31
ATOM	26	C29	TTB	2	15.200	33.030	69.849	-0.00	0.40
ATOM	27	C30	TTB	2	16.254	32.999	68.944	-0.00	0.39
ATOM	28	C32	TTB	2	17.316	32.127	69.141	-0.00	0.48
ATOM	29	C34	TTB	2	17.326	31.282	70.245	-0.00	0.62
ATOM	30	F36	TTB	2	18.351	30.438	70.433	-0.00	0.52
ATOM	31	C33	TTB	2	16.273	31.311	71.152	-0.00	0.62
ATOM	32	C31	TTB	2	15.209	32.185	70.955	-0.00	0.51
ATOM	33	C27	TTB	2	13.232	33.776	68.553	-0.00	0.06
ATOM	34	C24	TTB	2	12.173	34.657	68.357	-0.00	0.15
ATOM	35	C19	TTB	2	8.350	37.140	69.473	-0.00	0.07
ATOM	36	O22	TTB	2	8.431	38.373	69.525	0.00	0.23
ATOM	37	O21	TTB	2	7.170	36.528	69.074	0.00	0.20
ATOM	38	C25	TTB	2	6.157	36.738	70.054	-0.00	0.04
ATOM	39	O16	TTB	2	7.384	36.786	73.924	0.00	0.19
ATOM	40	H14	TTB	2	10.230	37.479	71.476	0.00	0.12
ATOM	41	H16	TTB	2	6.855	35.946	73.905	0.00	0.11

END

REMARK 4

REMARK TTP-B Computed low-energy docking mode-3

REMARK Computed Free energy of binding = -9.72kcal/mol

ATOM	1	C1	TTB	3	16.497	36.818	77.723	-0.00	0.50
ATOM	2	C3	TTB	3	15.398	36.382	76.989	-0.00	0.37
ATOM	3	C4	TTB	3	16.865	36.149	78.882	-0.00	0.68
ATOM	4	C7	TTB	3	14.666	35.272	77.408	-0.00	0.52
ATOM	5	C8	TTB	3	16.137	35.044	79.305	-0.00	0.74
ATOM	6	C12	TTB	3	15.041	34.602	78.574	-0.00	0.72
ATOM	7	C2	TTB	3	17.281	37.975	77.281	-0.00	0.43
ATOM	8	C5	TTB	3	17.913	37.972	76.042	-0.00	0.20
ATOM	9	C9	TTB	3	18.662	39.074	75.642	-0.00	0.26
ATOM	10	C13	TTB	3	18.782	40.175	76.482	-0.00	0.47
ATOM	11	C	TTB	3	19.594	41.362	76.055	-0.00	0.37
ATOM	12	F2	TTB	3	19.158	42.503	76.698	-0.00	0.23
ATOM	13	F3	TTB	3	20.905	41.128	76.411	-0.00	0.39
ATOM	14	F4	TTB	3	19.556	41.491	74.683	-0.00	0.18
ATOM	15	C10	TTB	3	18.150	40.181	77.719	-0.00	0.43
ATOM	16	C6	TTB	3	17.402	39.081	78.118	-0.00	0.61
ATOM	17	C11	TTB	3	13.506	34.832	76.586	-0.00	0.54
ATOM	18	O15	TTB	3	13.425	33.646	76.245	0.00	0.14
ATOM	19	N14	TTB	3	12.506	35.744	76.206	-0.00	0.31
ATOM	20	C17	TTB	3	11.364	35.307	75.490	-0.00	0.35
ATOM	21	C18	TTB	3	11.085	36.377	74.398	-0.00	0.27
ATOM	22	C20	TTB	3	12.345	36.921	73.732	-0.00	0.22
ATOM	23	C23	TTB	3	13.086	36.082	72.908	-0.00	0.25
ATOM	24	C26	TTB	3	14.229	36.554	72.273	-0.00	0.15
ATOM	25	C28	TTB	3	14.638	37.870	72.458	-0.00	0.18
ATOM	26	C29	TTB	3	15.842	38.359	71.790	-0.00	0.11
ATOM	27	C30	TTB	3	15.774	38.788	70.470	-0.00	0.13
ATOM	28	C32	TTB	3	16.915	39.253	69.830	-0.00	0.14
ATOM	29	C34	TTB	3	18.128	39.288	70.510	-0.00	0.22
ATOM	30	F36	TTB	3	19.230	39.736	69.889	-0.00	0.17
ATOM	31	C33	TTB	3	18.198	38.860	71.829	-0.00	0.32
ATOM	32	C31	TTB	3	17.055	38.395	72.471	-0.00	0.25
ATOM	33	C27	TTB	3	13.900	38.716	73.277	-0.00	0.16
ATOM	34	C24	TTB	3	12.756	38.242	73.910	-0.00	0.19
ATOM	35	C19	TTB	3	10.246	35.227	76.485	-0.00	0.52
ATOM	36	O22	TTB	3	9.666	36.259	76.846	-0.00	0.11
ATOM	37	O21	TTB	3	9.881	33.994	77.008	-0.00	0.17

ATOM	38	C25	TTB	3	8.461	33.878	77.034	-0.00	0.54
ATOM	39	O16	TTB	3	14.339	33.484	79.037	-0.00	0.10
ATOM	40	H14	TTB	3	12.604	36.740	76.451	0.00	0.07
ATOM	41	H16	TTB	3	13.868	33.718	79.880	-0.00	0.28

END

REMARK 4

REMARK TTP-B Computed low-energy docking mode-4

REMARK Computed Free energy of binding = -10.23kcal/mol

ATOM	1	C1	TTB	4	17.143	39.598	75.386	-0.00	0.31
ATOM	2	C3	TTB	4	17.445	38.517	76.209	-0.00	0.44
ATOM	3	C4	TTB	4	16.386	39.404	74.239	-0.00	0.23
ATOM	4	C7	TTB	4	16.986	37.239	75.892	-0.00	0.48
ATOM	5	C8	TTB	4	15.929	38.132	73.917	-0.00	0.28
ATOM	6	C12	TTB	4	16.224	37.051	74.737	-0.00	0.41
ATOM	7	C2	TTB	4	17.609	40.947	75.720	-0.00	0.27
ATOM	8	C5	TTB	4	16.917	41.727	76.641	-0.00	0.29
ATOM	9	C9	TTB	4	17.367	43.009	76.940	-0.00	0.16
ATOM	10	C13	TTB	4	18.503	43.512	76.315	-0.00	0.18
ATOM	11	C	TTB	4	18.985	44.897	76.631	-0.00	0.12
ATOM	12	F2	TTB	4	17.946	45.676	77.099	-0.00	0.09
ATOM	13	F3	TTB	4	19.942	44.796	77.619	-0.00	0.15
ATOM	14	F4	TTB	4	19.593	45.448	75.524	-0.00	0.03
ATOM	15	C10	TTB	4	19.194	42.733	75.396	-0.00	0.16
ATOM	16	C6	TTB	4	18.747	41.453	75.098	-0.00	0.22
ATOM	17	C11	TTB	4	17.321	36.115	76.808	-0.00	0.49
ATOM	18	O15	TTB	4	18.340	35.448	76.594	0.00	0.20
ATOM	19	N14	TTB	4	16.501	35.815	77.909	-0.00	0.35
ATOM	20	C17	TTB	4	16.864	34.795	78.823	-0.00	0.70
ATOM	21	C18	TTB	4	15.710	33.755	78.814	-0.00	0.52
ATOM	22	C20	TTB	4	14.449	34.240	78.105	-0.00	0.72
ATOM	23	C23	TTB	4	13.472	34.897	78.844	-0.00	0.25
ATOM	24	C26	TTB	4	12.320	35.366	78.223	-0.00	0.39
ATOM	25	C28	TTB	4	12.138	35.180	76.857	-0.00	0.61
ATOM	26	C29	TTB	4	10.923	35.673	76.211	-0.00	0.53
ATOM	27	C30	TTB	4	9.795	34.865	76.154	-0.00	0.51
ATOM	28	C32	TTB	4	8.638	35.328	75.541	-0.00	0.39
ATOM	29	C34	TTB	4	8.609	36.601	74.983	-0.00	0.25
ATOM	30	F36	TTB	4	7.491	37.046	74.388	-0.00	0.10
ATOM	31	C33	TTB	4	9.736	37.411	75.039	-0.00	0.29
ATOM	32	C31	TTB	4	10.895	36.948	75.654	-0.00	0.35
ATOM	33	C27	TTB	4	13.112	34.528	76.111	-0.00	0.36
ATOM	34	C24	TTB	4	14.265	34.061	76.735	-0.00	0.58
ATOM	35	C19	TTB	4	17.003	35.456	80.161	-0.00	0.75
ATOM	36	O22	TTB	4	16.055	36.094	80.636	-0.00	0.01
ATOM	37	O21	TTB	4	18.203	35.360	80.851	-0.00	0.28
ATOM	38	C25	TTB	4	18.897	36.603	80.797	-0.00	0.80
ATOM	39	O16	TTB	4	15.741	35.788	74.375	-0.00	0.06
ATOM	40	H14	TTB	4	15.628	36.342	78.054	-0.00	0.17
ATOM	41	H16	TTB	4	14.949	35.568	74.931	0.00	0.10

END

REMARK 4

REMARK TTP-B Computed low-energy docking mode-5

REMARK Computed Free energy of binding = -8.81kcal/mol

ATOM	1	C1	TTB	5	4.526	31.683	76.605	-0.00	0.33
ATOM	2	C3	TTB	5	5.097	32.667	75.804	-0.00	0.30
ATOM	3	C4	TTB	5	5.268	31.104	77.625	-0.00	0.41
ATOM	4	C7	TTB	5	6.410	33.080	76.022	-0.00	0.31
ATOM	5	C8	TTB	5	6.579	31.509	77.844	-0.00	0.56
ATOM	6	C12	TTB	5	7.152	32.494	77.050	-0.00	0.48
ATOM	7	C2	TTB	5	3.140	31.254	76.392	-0.00	0.29
ATOM	8	C5	TTB	5	2.845	29.923	76.117	-0.00	0.35
ATOM	9	C9	TTB	5	1.526	29.534	75.908	-0.00	0.32
ATOM	10	C13	TTB	5	0.504	30.475	75.970	-0.00	0.26
ATOM	11	C	TTB	5	-0.918	30.059	75.738	-0.00	0.19
ATOM	12	F2	TTB	5	-1.743	30.598	76.705	-0.00	0.04
ATOM	13	F3	TTB	5	-1.306	30.543	74.507	-0.00	0.17

ATOM	14	F4	TTB	5	-1.004	28.684	75.686	-0.00	0.23
ATOM	15	C10	TTB	5	0.798	31.805	76.246	-0.00	0.14
ATOM	16	C6	TTB	5	2.115	32.193	76.456	-0.00	0.17
ATOM	17	C11	TTB	5	6.976	34.145	75.150	-0.00	0.29
ATOM	18	O15	TTB	5	7.833	33.843	74.311	-0.00	0.18
ATOM	19	N14	TTB	5	6.540	35.476	75.264	-0.00	0.11
ATOM	20	C17	TTB	5	7.023	36.473	74.380	-0.00	0.14
ATOM	21	C18	TTB	5	7.909	37.429	75.225	-0.00	0.23
ATOM	22	C20	TTB	5	9.314	36.895	75.489	-0.00	0.35
ATOM	23	C23	TTB	5	10.230	36.867	74.443	-0.00	0.24
ATOM	24	C26	TTB	5	11.523	36.403	74.656	-0.00	0.30
ATOM	25	C28	TTB	5	11.908	35.965	75.918	-0.00	0.45
ATOM	26	C29	TTB	5	13.268	35.476	76.134	-0.00	0.47
ATOM	27	C30	TTB	5	13.473	34.177	76.583	-0.00	0.49
ATOM	28	C32	TTB	5	14.762	33.707	76.790	-0.00	0.61
ATOM	29	C34	TTB	5	15.852	34.538	76.551	-0.00	0.57
ATOM	30	F36	TTB	5	17.098	34.083	76.755	-0.00	0.57
ATOM	31	C33	TTB	5	15.650	35.837	76.103	-0.00	0.46
ATOM	32	C31	TTB	5	14.357	36.308	75.893	-0.00	0.40
ATOM	33	C27	TTB	5	11.000	35.995	76.969	-0.00	0.41
ATOM	34	C24	TTB	5	9.707	36.461	76.754	-0.00	0.36
ATOM	35	C19	TTB	5	5.817	37.174	73.834	-0.00	0.06
ATOM	36	O22	TTB	5	5.068	37.798	74.596	0.00	0.21
ATOM	37	O21	TTB	5	5.540	37.104	72.475	0.00	0.22
ATOM	38	C25	TTB	5	4.369	37.860	72.178	-0.00	0.01
ATOM	39	O16	TTB	5	8.474	32.873	77.308	-0.00	0.21
ATOM	40	H14	TTB	5	5.863	35.730	75.997	0.00	0.11
ATOM	41	H16	TTB	5	8.626	32.887	78.289	-0.00	0.09

END

Table 5
Atomic Interactions Between I7L and TTP-A

TTP-A Atom ¹	I7L Atom ²	Distance (Angstroms)	Interaction type
O2	Cys328 - SG	3.18	Charge
O3	Gly329 - N	3.62	Charge
C10	Trp168 - CB	3.34	Hydrophobic
O8	Asn171 - N	2.86	Hydrogen bond
C12	Met195 - SG	3.74	Hydrophobic
O25	Asn199 - OD1	3.26	Hydrogen bond
H17	Phe236 - O	1.86	Hydrogen bond
C24	Ile203 - CD1	4.79	Hydrophobic
C14	Met195 - SG	3.33	Hydrophobic
O2	Ser240 - OG	3.76	Hydrogen bond

1- Designations for atoms on TTP-A are as shown in FIG. 6

2- Designations for atoms in I7L are as shown in Table 2

5

Table 6
Atomic Interactions Between I7L and TTP-B

TTP-B Atom ¹	I7L Atom ²	Distance (Angstroms)	Interaction type
O21	Cys328 - SG	3.07	Electrostatic
C25	Met169 - CB	3.70	Hydrophobic
O22	His241 - N	3.08	Hydrogen bond
O15	Asn171 - N	2.87	Hydrogen bond
H14	Leu239 - O	2.20	Hydrogen bond
O16	Asn171 - ND2	3.50	Hydrogen bond
C26	Leu239 - CA	3.06	Hydrophobic
C27	Met195 - SD	3.24	Hydrophobic
C9	Trp168 - CE3	3.12	Hydrophobic
C5	Leu239 - CD1	3.97	Hydrophobic

1- Designations for atoms on TTP-B are as shown in FIG. 6

2- Designations for atoms in I7L are as shown in Table 2

10